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TABLE OF CONTENTS FIRST PAGE

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CONTENTS

Original Articles

Quantitative Studies of Experimental Production and Treatment of Acute Closed Cerebral Injury — PAGE

George M. Hass, M.D., and C. Bruce Taylor, M.D., Chicago 145

Amyotrophic Lateral Sclerosis

Tiffany Lawyer Jr., M.D., and Martin G. Netsky, M.D., New York 171

Group Therapy of Patients with Multiple Sclerosis

Max Day, M.D.; Elvira Day, B.A., and Rosalind Herrmann, B.A., Boston 193

Progressive Bulbar Paralysis Showing Heredofamilial Incidence and Intellectual Impairment

E. E. Robertson, M.B., Ch.B., M.R.C.P. Ed., D.P.M., Lond., Edinburgh, Scotland 197

Hemangiomas of the Pons

Karl Teilmann, M.D., Aarhus, Denmark 208

Aggression, Guilt and Cataplexy

Max Levin, M.D., New York 224

Retraction Nystagmus and Retraction of Eyelids Due to Arteriovenous Aneurysm of Midbrain

H. Askenasy, M.D.; H. Wijsenbeek, M.D., and E. Herzberger, M.D., Petah Tikva, Israel 236

Bilateral Encapsulated Subdural Effusion Complicating Bacterial Meningitis in Infancy

Joseph A. Epstein, M.D., and Sanford E. Goldzier II, M.D., New York 242

Society Transactions

Boston Society of Psychiatry and Neurology 250

Regular Departments

Abstracts from Current Literature 257

News and Comment 276

Books 279

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QUANTITATIVE STUDIES OF EXPERIMENTAL PRODUCTION AND TREATMENT OF ACUTE CLOSED CEREBRAL INJURY

GEORGE M. HASS, M.D.
AND
C. BRUCE TAYLOR, M.D.
CHICAGO

ACUTE expanding closed cerebral lesions in patients present many problems, related principally to pathogenesis of symptoms and choice of therapy. Much conflict of opinion about these matters has arisen because they cannot be studied in complicated human cases in a quantitative way. A method for the experimental production of acute closed cerebral lesions in animals has made it possible to conduct quantitative studies.[1] The method was refined so that discrete intracerebral lesions of desired volume could be reproduced in successive animals without interrupting the continuity of the calvaria or introducing variables incidental to mechanical trauma.[2]

This report is concerned with a description of the method and its use in the study of relations of volume per cent of cerebral damage to clinical manifestations, not only in untreated animals but also in animals treated with intravenous injections of hypertonic dextrose solution or surgical decompression.

METHODS

Instrument for Production of Cerebral Lesions.—Lesions of the brain were produced by creating a negative thermal gradient from the brain through the adjacent intact calvaria to a contiguous instrument cooled by expansion of gaseous carbon dioxide.

The apparatus consisted of two assemblies. One assembly governed the flow of carbon dioxide. The other was the hypothermal instrument for controlling the dimensions of lesions. A detailed description of the apparatus, parts of which are shown in Figure 1*A*, has been given elsewhere.[1] The essentials were as follows: Carbon dioxide was conducted to a needle valve at a pressure of 800 to 1,100 lb. per square inch (56 to 77 kg. per square centimeter). When the needle valve was open, carbon dioxide flowed into the hypothermal instrument and expanded proximal to the inner surface of a flat circular metal plate. The metal plate was cooled by the expanding gas. When the plate was placed against the external surface of the skull, heat was abstracted from the successive deepening layers of tissue, namely, periosteum, skull, dura, lepto-

From the Rush Department of Pathology, Presbyterian Hospital, in affiliation with the University of Illinois College of Medicine.

These studies were supported by a grant from the Otho S. A. Sprague Memorial Fund, and in part by funds provided under contract AF33(038)-25734 with the United States Air Force School of Aviation Medicine, Randolph Field, Texas.

1. Hass, G. M., and Taylor, C.: A Quantitative Hypothermal Method for the Production of Local Injury of Tissue, Arch. Path. **45**:563, 1948.

2. Taylor, C. B.; Hass, G. M., and Maloney, J. E.: Relations Between Volumes of Closed Hypothermal Cerebral Lesions and Symptoms in Rabbits, Arch. Path. **47**:450, 1949.

meninges, cerebral cortex, subcortical white matter, and deep intracerebral structures. The effective negative thermal gradient from tissue to plate was almost equal along any line perpendicular to the applied surface of the plate. The effective cross-sectional area of the negative thermal gradient was, therefore, almost equal to the surface area of the plate in contact with tissue and could be varied by use of plates of different diameters (5 to 20 mm.; Fig. 1*A*). The effective depths

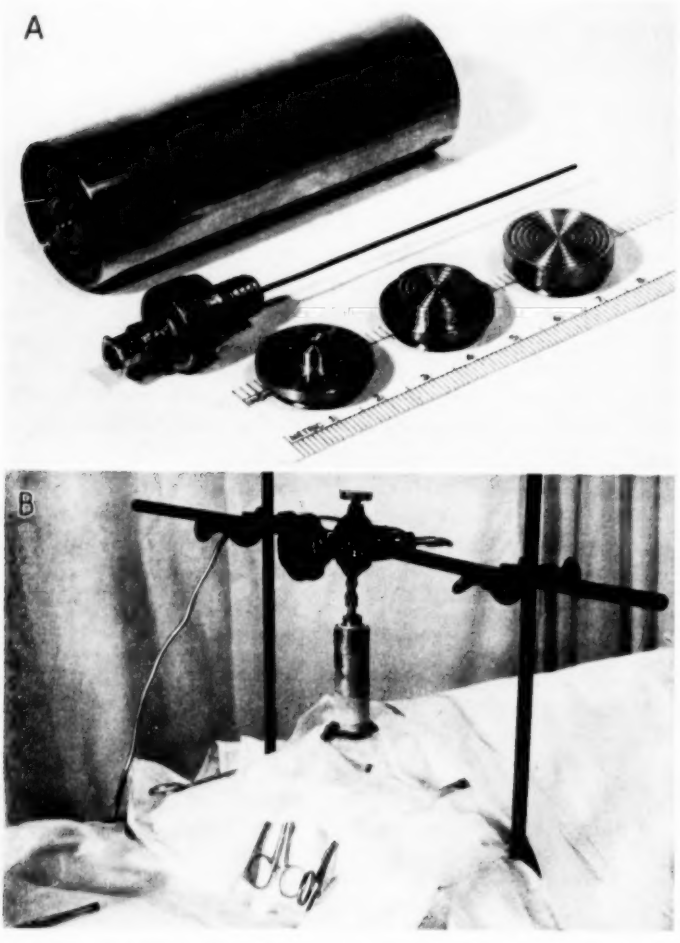

Fig. 1.—*A*, three principal parts of the hypothermal instrument. The long needle, through which carbon dioxide is conducted into the expansion chamber, fits into one end of the cylinder. The three freezing plates, which are of different dimensions, fit interchangeably into the other end of the cylinder, forming a part of the wall of the expansion chamber.

B, hypothermal instrument in operation. The hypothermal plate is frozen firmly to the intact external table of the calvaria of a rabbit. Heat is being abstracted from the right cerebral hemisphere within the closed cranial vault. Control of the flow of heat leads to the production of a cerebral lesion of desired volume.

(0 to 13 mm.) of the negative thermal gradient were governed by control of duration of flow of carbon dioxide through the instrument under standard conditions while the cooling plate was

in contact with tissue. The effective volumes (about 0 to 4000 cu. mm.) of the negative thermal gradient were dependent, therefore, upon the diameter of the applied circular cooling plate, the duration of flow of carbon dioxide through the instrument, and adherence to standard conditions.

General Use of Instrument in Production of Cerebral Lesions.—Experiments were done on albino rabbits, 3 to 6 months of age and weighing 4 to 6 lb. (1.8 to 2.7 kg.). After induction of anesthesia with ether, the animal was fastened to the operating table in the prone position. A midline incision about 1 in. (2.5 cm.) long was made, aseptically, in the scalp over the superior longitudinal synostosis. The scalp was then reflected laterally to expose the superior surface of the occipital, frontal, and parietal bones. The cooling plate of desired diameter was then screwed into the end of the hypothermal instrument. The surface of the plate was then immersed in a sterile 10% aqueous solution of gelatin at 50 C. The cooling plate was then placed firmly against the skull to the right or to the left of the midline over the part of the cerebrum in which the lesion was to be produced. After it was certain that the gelatin had made a liquid seal between the cooling plate and the periosteum, excess gelatin was wiped away. Carbon dioxide was then jetted periodically by manual control of the needle valve against the inner surface of the cooling plate (Fig. 1*B*). The duration of each jet and the interval between jets were timed with a metronome at 0.1 and 0.2 second. When a lesion of desired volume had been produced, the instrument and tissue were allowed to gain heat from the environment. Within five minutes the tissue and cooling plate, which had been securely frozen together, spontaneously separated. The scalp was then closed with silk and anesthesia discontinued.

Lesions over a wide range with respect to location, breadth, depth, and volume were produced in the superior convexity of the occipital, parietal, and frontal lobes of cerebral hemispheres. Most lesions of great surface area, depth, and volume were made in parietal areas because of the less convex contour of the skull in these regions. Diameters of lesions varied from 4 to 25 mm.; depths, from 0.5 to 7 mm., and volumes, from about 100 to 3,000 cu. mm.

General Postoperative Clinical Observations.—After production of lesions periodic observations were made. Duration of recovery from anesthesia was recorded. Attempts were made to disclose motor paralyses and conspicuous changes in behavior. If the animal regained consciousness after the operation, it was watched for signs of onset of cerebral symptoms. The time of onset of symptoms and the duration of life following production of lesions were recorded. Five types of clinical courses were recognized.

Postmortem Studies.—Postmortem studies were made in all cases. In most experiments animals which survived were killed 24 hours after the production of the final lesion. In special experiments animals were kept for as long as four weeks to determine histopathologic changes during healing of lesions. The condition of the scalp and calvaria was noted. The bone over each lesion was inspected, and blocks of the calvaria were prepared for microscopic study. The brain was removed by dissection, severed from the spinal cord at the foramen magnum, and fixed in 10% formalin. After fixation for 48 to 72 hours, a transverse incision was made through the medulla at the posterior angle of the fourth ventricle. After determination of volume per cent of cerebral damage, blocks were taken for microscopic study.

Determination of Volume per Cent of Brain Occupied by Lesions.—After fixation in formalin, the volume of the brain, in cubic millimeters, was determined by calculations from data on the weight of the brain in air and when immersed in distilled water. The volume of each cerebral lesion was then determined as follows: A template covering the subarachnoidal surface area of the lesion was prepared and transferred to graph paper, with transverse and vertical lines at intervals of 1 mm. The number of squares within the outline of the template was counted. This gave the surface area of the lesion in square millimeters. The lesion was then bisected in an axis perpendicular to the maximum diameter of the lesion. The maximum depth of the lesion was then measured to an accuracy of 0.25 mm. The product of the surface area and the depth was then taken as a standard approximation to the volume of the lesion. The volume per cent of cerebral damage was calculated as the ratio of the volume of the lesion to the volume of the brain.

Determination of $ML\%$ in Untreated Animals.—One hundred four rabbits were used. Single acute unilateral lesions or multiple acute simultaneous bilateral lesions were produced in various

frontal, parietal, and occipital regions. The lesions varied greatly in breadth, depth, and volume. Three ranges in volume per cent of cerebral damage were sought for. The low range was that within which all animals, 46 in number, survived. The high range was that within which all animals, 9 in number, died. The intermediate range encompassed all volumes per cent of cerebral damage between the minimum lethal volume per cent and the maximum survivable volume per cent. Forty-nine animals were in this series. Twenty-nine survived, and 20 died. The average volume per cent of cerebral damage was calculated for the two groups. The average of these values was regarded as the volume per cent of cerebral damage which might be expected to be lethal for 50% of a large group of animals. This value was defined as MLV_{50}.

Determination of Relations of Symptoms to Volume per Cent of Acute Cerebral Damage in Untreated Animals.—One hundred four animals used for the determination of MLV_{50} were studied. The nature of recovery from the anesthesia used for the operation was noted. Recovery was regarded as normal when the animal promptly regained normal activity. It was regarded as delayed if the animal remained stuporous for an hour or so before regaining normal activity. The record of no recovery was made if the animal failed to regain consciousness. The time of onset of symptoms of cerebral origin was recorded. The principal symptoms were stupor, coma, and convulsions. The duration of life after production of cerebral lesions and after onset of each symptom was also recorded. These data were analyzed and five types of clinical courses defined. Correlations were then made between the type of clinical course followed by each animal and the volume per cent of cerebral damage.

Determination of Rate of Onset and Subsidence of Factors Responsible for Symptoms Following Production of Acute Cerebral Lesions.—Closed intracerebral lesions were produced by the usual method except that multiple successive lesions were made in each animal at chosen intervals of time.[3] The first lesion (Lesion 1) was made in the left occipitoparietal region, care being taken to produce a sublethal lesion. The scalp was then closed with silk sutures. If the animal survived, the procedure was repeated after the lapse of a chosen interval of time, when a second lesion (Lesion 2) was made in the right occipitoparietal region. Lesions 3, 4, 5, and 6 were then produced successively at the same spaced intervals of time in the left and right parietal, and left and right frontal regions, respectively. In most instances animals did not survive the complete series, so that the number of lesions varied from two to six.

There were four groups of animals. Successive cerebral lesions were produced at intervals of 24 hours in 12 rabbits, 48 hours in 12 rabbits, 72 hours in 4 rabbits, and 96 hours in 4 rabbits. After the production of each lesion, clinical observations were made, and the type of clinical course was recorded.

If an animal lived 24 hours after production of a lesion, it was regarded as a survivor in accordance with experience with animals having acute single or multiple simultaneous lesions. All experiments, therefore, were terminated either by death from lethal lesions or by killing the animal 24 hours after production of the final lesion. The volume per cent of cerebral damage was then determined as the ratio of the sum of volumes of individual lesions to the volume of the brain. These data represented the effects of increments of cerebral damage spaced at 24, 48, 72, and 96 hours. The rate of onset and subsidence of factors responsible for severe cerebral symptoms and death were determined indirectly in terms of clinical effects of increments in cerebral damage. Control data were made available by the large series of animals with acute single or multiple simultaneous lesions. Maximum tolerated limits of cerebral damage were defined, and a suitable method for extensive closed cerebral ablation with low mortality was established.

Determination of Value of Intravenous Administration of Hypertonic Dextrose Solution in Treatment of Animals with Acute Closed Cerebral Lesions.—Twenty-four animals with acute closed cerebral lesions were treated by intravenous administration of 10 or 25% aqueous solutions of dextrose (Table 2). The dextrose was given in a vein of the ear with the head immobilized. The rate of administration, controlled by a mercury-drop displacement method, varied from as much as 50 ml. per minute, when single injections were given, to 6 to 8 ml. per hour, when

3. Taylor, C. B.; Hass, G. M., and Maloney, J. E.: Quantitative Study of the Effects of Multiple Successive Closed Cerebral Lesions, Arch. Path. **48**:195, 1949.

TABLE 1.—*Relations of Volume per Cent of Cerebral Damage, Type of Clinical Course, and Duration of Life*

Experiment No.	Volume per Cent of Cerebral Damage	Clinical Type	Duration of Life, Hr.*	Experiment No.	Volume per Cent of Cerebral Damage	Clinical Type	Duration of Life, Hr.*
16	1.3	1	S	25	10.3	3	7
20	3.6	1	S	135	10.4	1	S
2	3.7	1	S	59	11.1	1	S
60	3.8	1	S	122	11.3	1	S
18	3.8	1	S	107	11.4	1	S
67	4.1	1	S	100	11.5	4	3
62	4.1	1	S	102	11.7	1	S
6	4.2	2	S	57A	11.7	1	S
62	4.2	1	S	137	11.9	1	S
15	4.2	1	S	131	12.2	3	8
51	4.3	1	S	75A	12.4	1	S
17	4.3	1	S	133	12.6	1	S
21	4.3	1	S	136	12.7	1	S
43	4.5	1	S	149	12.8	3	20
112	4.5	2	S	111	13.0	5	S
41	4.6	2	S	154	13.5	2	S
70	4.7	1	S	139	13.5	4	5
127	4.9	1	S	97	13.6	3	12
36	5.0	1	S	19	13.6	1	5
38	5.4	1	S	120	14.1	1	S
69	5.5	1	S	140	14.3	1	S
86	5.7	2	S	161	14.6	4	3
85	6.0	1	S	155	14.9	5	S
129	6.1	1	S	98	15.0	3	24
111	6.1	2	S	105	15.0	1	S
42	6.4	2	S	123	15.2	1	S
83	6.8	1	S	126	15.3	3	6
106	6.9	1	S	138	15.7	3	6
61	7.0	1	S	99	15.8	3	25
40	7.2	1	S	81	15.9	3	2
116	7.6	1	S	156	16.1	3	4
117	7.7	1	S	158	16.2	1	S
3	7.8	1	S	160	16.4	3	4
30	7.9	1	S	121	16.4	1	S
36	7.9	1	S	104	16.6	2	S
1	8.0	1	S	141	16.9	3	3
22	8.0	1	S	159	17.2	5	S
39	8.2	1	S	90A	17.4	2	S
61	8.4	1	S	128	17.5	1	S
124	8.8	1	S	58A	17.7	3	11
84	8.9	1	S	92A	17.8	5	S
132	9.0	1	S	152	18.0	3	9
14	9.1	1	S	125	18.0	1	S
68	9.1	1	S	144	18.5	3	3
9	9.3	1	S	157	18.7	3	4
114	9.4	1	S	143	18.7	3	3
44	9.4	3	7	153	19.1	3	3
113	9.5	3	5	145	19.8	4	2
76	9.6	2	S	142	20.3	3	14
108	9.6	1	S	151	21.3	3	5
10	10.1	1	S	130	23.6	3	8
110	10.2	1	S	7	32.5	3	4

* S indicates the animal survived.

injection was continuous.[4] The time after operation, at which injections were given, the duration of administration, and the amounts injected into each animal are shown in Table 2.

All experiments were terminated by death from cerebral injury within 24 hours or by killing the animal at the end of 24 hours. The volume per cent of cerebral injury was then determined in the usual way. These values were compared with those obtained in the untreated, control animals with similar lesions, and conclusions concerning the effect of intravenous administration of hypertonic solution of dextrose upon the mortality rate were drawn.

Determination of Value of Surgical Decompression in Treatment of Animals with Acute Closed Cerebral Lesions.—Three groups of animals were treated by surgical decompression, with removal of bone flaps by the use of a rotary saw.[4]

TABLE 2.—*Relations of Volume per Cent of Cerebral Damage to Survival of Animals Treated with Intravenous Administration of Dextrose*

	Intravenous Therapy After Production of Lesions			
Volume per Cent of Cerebral Damage	Postoperative Method of Intravenous Administration of Dextrose	Concentration of Dextrose, %	Dose, Ml.	Duration of Life After Production of Lesions, Hr.*
8.9	Continuous infusion	25	177	23
11.0	Continuous infusion	25	30	4
12.1	Immediate single infusion	10	50	S
12.6	Continuous infusion	25	178	S
12.8	Delayed single infusion 1½ hr. p. o.	10	50	3
13.3	Continuous infusion	25	151	S
14.5	Immediate single infusion	10	17	S
14.6	Immediate single infusion	10	50	10
14.7	Two infusions at 0 and 1 hr. p. o.	25	50	2
14.9	Continuous infusion	25	12	2.25
16.3	Two infusions at ½ and 1 hr.	10	45	6
16.7	Delayed single infusion 1 hr. p. o.	10	17	3.75
16.9	Immediate single infusion	10	50	S
17.5	Continuous infusion	25	168	S
18.0	Continuous infusion	25	64	15
18.4	Continuous infusion	25	44	S
18.6	Four infusions at 0, 1, 2, 3 hr. p. o.	10	55	4
19.3	Immediate single infusion	10	50	6.5
19.5	Continuous infusion	25	182	S
19.6	Continuous infusion	25	20	2.75
19.7	Continuous infusion	25	12	1.25
21.2	Immediate single infusion	10	50	2.25
24.7	Continuous infusion	25	5	0.75
30.0	Continuous infusion	25	4	0.75

* S indicates the animal survived.

Group 1 consisted of 47 animals with unilateral or bilateral lesions (Table 3). Surgical decompression was done within 30 to 45 minutes after production of cerebral lesions. Bone flaps were made immediately over the lesions. The area of bone removed over each lesion was usually one-fourth to one-half the area of the cortical surface of the lesion (Table 3).

Group 2 consisted of four animals with unilateral lesions (Table 4). Surgical decompression was done within 30 to 105 minutes after production of lesions. Bone flaps were removed over the cerebral hemisphere contralateral to the location of the lesion.

Group 3 consisted of 14 animals with unilateral or bilateral lesions (Table 4). Surgical decompression was delayed one to six hours, until the postoperative onset of stupor or convulsions. These symptoms were regularly indicative of a fatal prognosis in untreated animals. Decompression had to be done rapidly, because death often promptly followed the onset of symp-

4. Taylor, C. B.; Hass, G. M., and Maloney, J. E.: Acute Closed Cerebral Lesions Treated by Injection of Hypertonic Dextrose Solution and by Surgical Decompression: A Quantitative Study, Arch. Path. **48**:525, 1949.

TABLE 3.—*Relations of Volume per Cent of Cerebral Damage to Survival of Animals Treated by Surgical Decompression over Each Lesion 30 to 45 Minutes After Production of Lesion*

Dimensions of Parietal Lesions				Dimensions of Decompressions			
Right		Left					
Surface Area, Sq. Mm.	Depth, Mm.	Surface Area, Sq. Mm.	Depth, Mm.	Right Area, Sq. Mm.	Left Area, Sq. Mm.	Volume per Cent Cerebral Damage	Duration of Life After Production of Lesions*
154	4.0	...	...	105	...	9.8	S
243	5.0	...	...	142	...	10.0	S
228	5.0	...	...	149	...	11.0	S
149	4.5	170	5.0	61	100	12.5	S
351	5.0	...	...	138	...	12.6	S
290	4.5	...	...	150	...	13.1	S
325	5.0	...	...	141	...	13.3	S
355	5.0	...	...	125	...	13.5	S
342	5.5	...	...	143	...	14.0	S
327	5.0	...	...	123	...	14.2	S
385	5.0	...	...	223	...	14.6	16
328	4.0	71	4.0	160	...	14.7	10
387	5.0	...	...	142	...	14.9	S
390	5.0	...	...	132	...	15.0	S
330	5.0	...	...	141	...	15.0	7
434	5.0	...	...	218	...	15.4	4
362	5.0	...	...	118	...	15.6	S
407	5.0	...	...	142	...	15.7	S
410	5.0	...	...	181	...	16.4	S
343	6.0	...	...	198	...	16.5	S
369	6.0	...	...	154	...	16.6	14
362	3.0	324	3.5	94	110	17.6	4
54	4.5	432	4.5	...	109	17.8	7
281	5.0	222	4.5	41	78	18.3	S
427	7.0	...	...	135	...	19.0	S
437	5.5	...	...	110	...	20.0	9
312	4.0	324	4.0	88	91	20.4	5
542	5.5	...	...	160	...	20.6	S
439	6.0	...	...	138	...	21.2	9
448	6.0	...	...	120	...	21.3	S
331	5.0	314	3.0	92	100	22.4	13
461	6.5	...	...	144	...	23.4	S
306	5.0	329	4.0	94	85	23.5	S
324	5.0	309	5.0	56	52	24.0	7
294	4.0	285	6.0	65	47	24.0	S
338	5.0	318	4.5	105	128	26.0	18
321	6.0	324	5.5	131	94	26.5	S
439	3.5	420	5.0	83	75	27.7	7
388	5.0	360	4.5	150	95	28.5	3
305	4.2	315	4.3	84	94	29.2	16
416	4.0	420	4.0	80	89	29.3	3
499	3.5	408	4.2	118	101	29.6	4
360	4.5	358	5.0	107	99	29.9	S
350	5.5	350	5.5	112	118	32.3	S
310	7.0	250	7.0	119	125	32.7	S
375	6.0	393	6.0	92	101	33.5	3
456	7.5	403	7.8	129	104	51.2	4

* S indicates survival; numerals indicate number of hours animal lived.

toms. It was possible to do a decompression in only 8 of the 14 animals. Five died before the decompression could be undertaken. One survived without symptoms. Decompression was done just over the lesions, the bone removed having a surface area equal to one-fourth to one-half the surface area of the subjacent cortical lesion.

Animals which survived were killed at the end of 24 hours. The volume per cent of cerebral damage was determined in the usual way. By analysis of the data we were able to compare, first, the relative merits of homolateral and contralateral decompression and, second, the relative merits of immediate and delayed homolateral decompression.

RESULTS

Limitations in Measurement and Reproduction of Closed Craniocerebral Lesions.—The method used in these experiments eliminated variables, such as

TABLE 4.—*Relations Between Volume per Cent of Cerebral Damage and Survival of Animals Treated by Surgical Decompression*

Volume per Cent of Cerebral Damage	Time Interval Between Production of Lesions and Onset of Symptoms, Hr.		Time Interval Between Production of Lesions and Surgical Decompression, Hr.		Duration of Life After Production of Lesions*
	Stupor	Convulsions	Over Lesion	Contralateral to Lesion	
11.7	...	....	....	1.50	8
12.6	...	....	....	0.50	4.00
13.5	5.0	....	....	1.75	5.25
15.2	5.0	....	....	1.50	5.50
12.3	...	1.5	....	....	1.50
12.4	...	....	....	....	8
14.8	...	1.5	....	....	1.50
17.0	2.0	2.75	....	....	2.75
19.1	...	1.00	....	....	1.00
19.2	4.0	....	4.0	....	8
19.4	...	3.50	3.50	...	8
19.6	4.0	....	4.00	....	8
20.5	...	1.00	....	....	1.00
21.0	1.5	....	1.50	....	1.75
21.5	6.0	....	5.00	....	8
22.2	...	1.00	1.00	....	8
24.7	1.5	....	1.75	....	8
49.4	...	0.75	1.00	....	2.25

* 8 indicates survival; numerals indicate duration of life, in hours, after production of lesions.

concussion, cranial fracture, diffuse cerebral injury, or craniotomy, with their numerous complications. Other variables, such as location, dimensions, and character of lesions, were only partly controlled. There were limits as to location in which large volumes of cerebral damage could be conveniently produced. Most suitable locations were beneath the superior planar or superior lateral convex surface of the cranial vault. The lateral, inferior, and medial aspects of cerebral hemispheres were not selectively damaged because of technical difficulties in accurate reproduction of lesions in successive animals.

Dimensions of lesions of certain types were reproduced with reasonable accuracy in successive experiments (Fig. 2). The range of error in reproduction of lesions of medium or large diameter (about 15 to 25 mm.), depth (about 3 to 5 mm.), and volume (about 500 to 2,000 ctu. mm.) was no greater than ±10% of the desired values. Large errors frequently occurred when attempts were made to reproduce lesions of large or medium diameter (15 to 25 mm.), small depth (0.5

to 1.0 mm.), and very small volume (75 to 200 cu. mm.). In general, the range of error in reproduction of a lesion increased with increasing divergence of values for diameter and depth.

Acute lesions, at the same time interval after production, were similar but not always identical in appearance (Fig. 3). The amount of hemorrhage, necrosis, and edema varied. These variations were encountered, at times, even when the method of production and resulting dimensions of lesions were identical. Since there was no hemorrhage beyond the limits of the lesion, except when a wall of a lateral

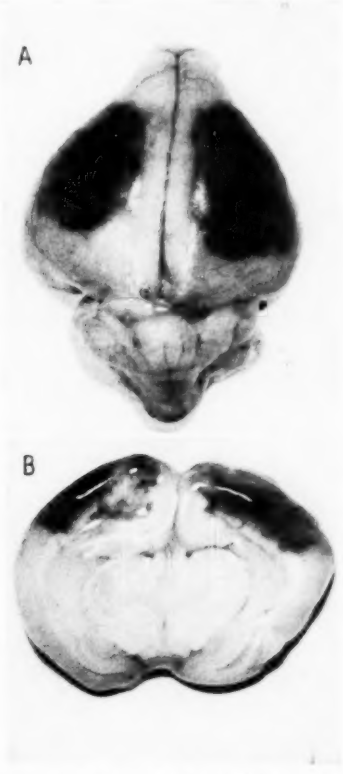

Fig. 2.—*A*, two acute symmetrical lesions in the parietal region. The margins of the lesions are sharp. Congestion and edema are conspicuous in this instance, while gross hemorrhage is insignificant in quantity. The clinical course of this animal was Type 3.

B, sagittal section of two acute symmetrical lesions in the parietal region. The margins and base of each lesion are sharp. There are congestion, edema, and discrete perivascular hemorrhage within the limits of each lesion. The clinical course of this rabbit was Type 3.

ventricle had been destroyed, the slight variation of bleeding within the boundaries of lesions would seem to be unimportant. However, it was doubtless contributory to variable clinical manifestations caused by comparable volumes per cent of acute cerebral damage in the same location in different animals. The same comment may be made concerning minor variations in the amount of cerebral necrosis within lesions, as well as of edema in and around lesions.

There were several sources of error in measurements of dimensions of lesions. There was little error in the method of measurement of the volume of the brain. The differences, however, between the volume, as measured, and the true normal volume were, at times, considerable. Fixation of the brain in formaldehyde decreased its volume, but it seemed probable that the standard duration of fixation eliminated

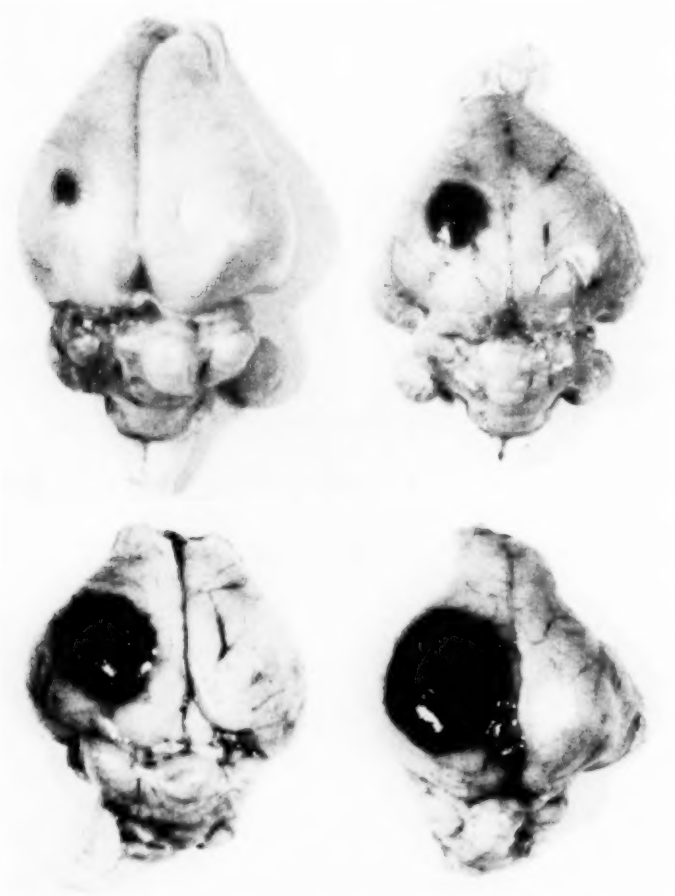

Fig. 3.—Four acute lesions, of different dimensions, in the left parietal area. All are sharply defined. Note the restriction of congestion, edema, and hemorrhage to the site of each lesion. The clinical courses of the four rabbits were Types I, II, III, and IV, respectively, in accord with the increasing volume of the lesions.

significance of this source of error. The presence of a lesion also changed the "normal" volume of the brain. When a lesion was acute, there was an increase in cerebral volume because of edema and hemorrhage within the lesion. These factors necessarily varied, increasing, in general, with increase in the volume per cent of acute cerebral damage. As lesions became older, edema subsided, hemorrhage

resorbed, and degenerated cerebral tissue disappeared, leaving a contracted scar. In these instances the cerebral volume was reduced to below "normal." However, the measured volume of the lesion decreased with age at a much more rapid rate than the measured volume of the brain. The over-all effect of old healing lesions was to reduce the value for the actual volume per cent of cerebral damage. This effect was important only in prolonged experiments, especially those in which successive lesions were produced in the same animal at intervals of 24, 48, 72, and 96 hours.

The volume of each lesion was never accurately measured. The measurements of the surface area and depth were accurate because each lesion was very sharply defined at its margins (Figs. 2 and 3). The product of these measurements was only an approximation to the true volume because lesions were not strictly cylindrical. The submeningeal and intracerebral bases were usually convex, and the diameter of lesions diminished slightly with increasing depth (Fig. 2*B*). In general, therefore, the calculated volumes were somewhat greater than the actual volumes.

For the reasons given, it was necessary to restrict critical comparison of one experiment with another to instances in which lesions did not differ greatly in volume and age. In addition, uncontrolled variables were such that we have attached no significance to data which fail to take into account a ± 10% range of error in measurement of the volume per cent of cerebral damage.

Types of Postoperative Clinical Courses.—Five types of postoperative clinical courses were recognized.

One clinical course (Type 1) consisted of rapid asymptomatic recovery from the anesthesia, with a subsequent asymptomatic course.

A second clinical course (Type 2) was characterized by delayed recovery from anesthesia, with persistence of stupor for less than two hours, followed by complete asymptomatic recovery.

A third clinical course (Type 3) was characterized by a well-defined sequence of signs and symptoms. Usually, there was a slightly delayed recovery from the anesthesia. Then the animal became ambulatory and behaved normally for a period varying from 2 to 10 hours. After this period of normal behavior, there was an onset of stupor, followed by coma, terminated within two hours by convulsions and death. This clinical course was critical prognostically because all animals which recovered consciousness after the postoperation and then after a period of normal behavior lapsed into a stuporous state died within 25 hours after the time of production of the cerebral lesion.

A more rapidly progressive clinical course (Type 4) was characterized by incomplete recovery from anesthesia with persistence of unconsciousness, terminated by convulsions and death, usually within two to six hours after production of the lesion.

The final type of clinical course (Type 5) was seldom observed in acute experiments but was common among animals subjected to progressive cortical ablation by successive lesions produced at intervals of 24, 48, 72, and 96 hours. These animals never regained normal behavior after operation. They remained sluggish and

responded to stimuli by hopping slowly away. They did not eat and tended to remain in semireclining postures until they were near death from dehydration and inanition.

No well-defined hemiparesis, paraplegia, or other localizing neurological sign was encountered in any animal.

Pathologic Findings.—Immediately after production of a lesion there was no gross or microscopic change in the periosteum, bone, or dura. There were engorged vessels and pericapillary hemorrhages in the leptomeninges and brain (Fig. 2). These changes were invariably restricted to the site of the lesion. Significant diffuse bleeding into the subarachnoid space or ventricles occurred only in instances in which massive deep lesions involved ventricular walls. The rare cases of this type were eliminated from our experiments. Otherwise, bleeding into the subarachnoid space was negligible and restricted within the boundaries of the lesion. Hemostasis was spontaneous and efficient after the immediate postoperative period.

During the first few hours after production of lesions there were slight gross changes in the periosteum, bone, and dura at the site of the lesions. The subdural spaces within the limits of the zone of injury gradually became obliterated as fibrinous exudate bound the leptomeninges to the dura. There was no consistent evidence of continuous oozing of blood into the subarachnoid space or intracerebral part of the lesion (Fig. 3). Edema, however, did develop progressively. It was mild in the periosteum, dura, and leptomeninges. It was prominent in the brain within and adjacent to the volume of damaged cerebral tissue.

Microscopic study of lesions during the first few hours after production showed early necrosis of cells, vasodilatation, intravascular thrombi, edema, interstitial hemorrhage, and infiltration of few inflammatory cells. These changes, though mild in the periosteum and dura, were conspicuous in the bone marrow of the calvaria. Fibrous and osseous matrices were surprisingly resistant to change, even though cells had apparently been killed. Sections of the brain showed vasodilatation, intravascular thrombi, perivascular hemorrhage, and necrosis of neural structures. Ganglion cells disappeared rapidly. Endothelial cells, fibrocytes, and neuroglia cells were more resistant and often seemed to persist as structurally unimpaired units. Infiltration with polymorphonuclear leucocytes and macrophages was retarded and mild. There was no suppuration or liquefaction necrosis (Figs. 4 and 5).

Gross study of the evolution of lesions over a period of several weeks showed apparent return of periosteum and bone to normal. The leptomeninges became firmly fixed by fibrous adhesions to the dura and cerebrum within the local limits of the boundary of the lesion. The cerebral lesions contracted progressively, so that by the end of five weeks large purplish-red, acute lesions had been converted to small yellow, puckered glial scars, enclosing soft masses of degenerated cerebral tissue and cysts.

Microscopic study showed slow progressive healing over a period of several weeks. Sections of the calvaria showed a peculiar formation of osteoid tissue in relation to the residual acellular framework of "nonviable" bone. The dura, thickened by fibrosis, became fused with the leptomeninges, which, in turn, were bound by fibrous adhesions to the surface of the healing cortical lesion. The acute inflammatory and neuronal degenerative changes subsided without suppuration

within the first few days. Then, macrophages, laden with lipids derived from disintegrating neurons, became conspicuous. The process of resorption, phagocytosis, and gliosis was very slow. All ganglion cells and axons disappeared. Reparative processes finally converted the volume of injured cerebral tissue into a lesion which closely resembled certain types of healed infarcts of the human brain.

Relations of Clinical Course to Volume per Cent of Acute Cerebral Damage in Untreated Animals.—The type of clinical course could usually be correlated with a range in volume per cent of acute cerebral damage (Table 1). The variable distribution of the damage within the extraventricular limits of the superior convexity of the cerebrum was not important. Also, clinical findings in animals with large unilateral lesions were comparable with those in animals with small bilateral lesions leading to the same total volume per cent of damage. Clinical courses Type 1 or Type 2 were followed when the animals had 1.3 to 9.4 vol. % of cerebral damage. The animals recovered normal postoperative behavior either very

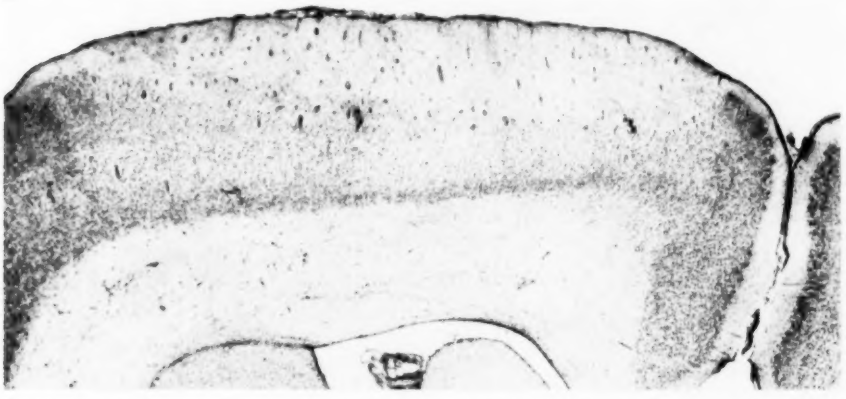

Fig. 4.—Low-power photomicrograph of a sagittal section of a lesion in the parietal lobe of a rabbit brain. This lesion, which is very small, was 12 hours old. Note the sharp margins and the convex base of the lesion in the midzone of the cortical gray matter. All nerve cells within the limits of the lesion have disappeared, but there is no other significant disintegration of structure. Perivascular hemorrhage and leucocytic infiltration are inconspicuous.

promptly or after slightly prolonged recovery from the anesthesia. Thereafter they had no significant signs or symptoms. Of the 46 animals in this group, 6 had a prolonged postoperative recovery period (15 to 30 minutes) after discontinuation of the anesthesia (Type 2). The remainder recovered promptly (Type 1). Clinical courses Type 1 to Type 5 were observed among animals with 9.4 to 18.5 vol. % of cerebral damage. Of these 49 animals, 25 followed clinical courses Type 1 or Type 2. Clinical course Type 3 was observed in 17 animals. These, after a slight postoperative delay in recovery from anesthesia, returned to a state of normal behavior but thereafter lapsed into stupor, terminated by coma and death. The duration of normal postoperative behavior varied from 1 to 20 hours and the postoperative duration of life varied from 2 to 25 hours. Clinical course Type 4 was encountered in three animals. They failed to regain full consciousness after operation. Stupor persisted and was followed by coma and death three to five hours

after the operation. Clinical course Type 5 was observed in four animals, with 13.0 to 17.8 vol. % of cerebral damage. These animals persisted in a static postoperative stupor and exhibited no desire to eat or drink. This condition remained unchanged for at least two days, at which time it was apparent they would eventually die of causes other than acute cerebral damage.

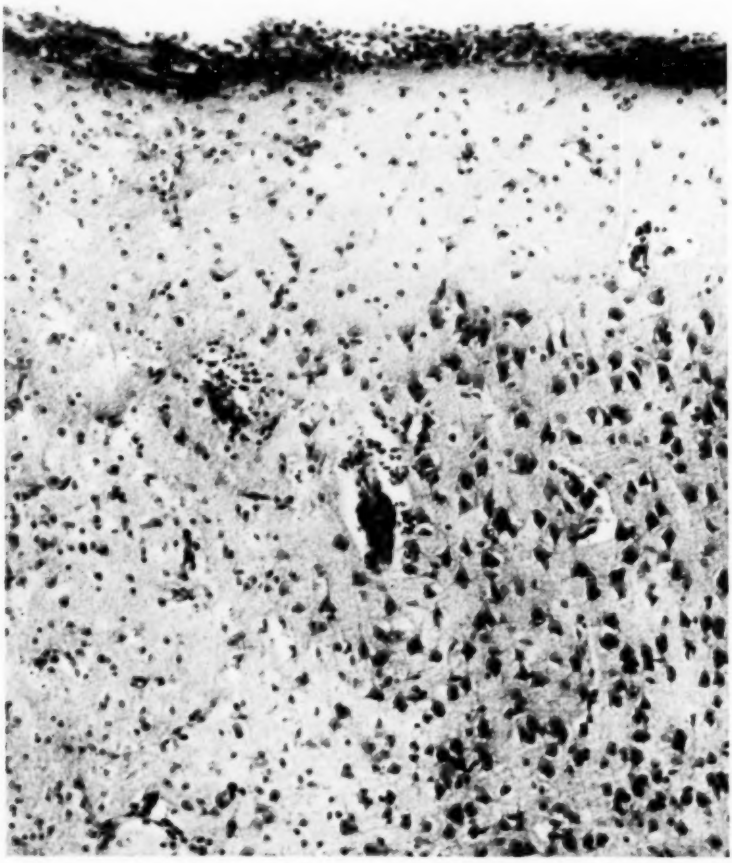

Fig. 5.—Photomicrograph showing cortical aspect of the margin of an acute lesion. There is mild hemorrhage in the pia-mater. Congestion, edema, and perivascular hemorrhage are conspicuous within the limits of the lesion. Cortical ganglion cells have disintegrated. Several glia cells, fibrocytes, and endothelial cells of capillaries remain. Infiltration of the zone of injury with inflammatory cells is negligible.

All animals, nine in number, with more than 18.5 vol. % of cerebral injury died within 2 to 14 hours after operation. Clinical course Type 3 was followed by eight animals. One animal followed clinical course Type 4.

The following conclusions were drawn concerning the effect of single unilateral or multiple simultaneous unilateral or bilateral acute lesions in untreated animals (Table 1): When the quantity of cerebral damage was less than 9.4 vol. %, there

were no significant signs or symptoms. When the quantity of cerebral damage was within the range of 9.4 to 18.5 vol. %, the probability of survival was about one-half, diminishing somewhat with increasing values within the range (Fig. 6). When the quantity of cerebral damage was greater than 18.5 vol. %, no animal survived. The clinical counterpart of minimum lethal cerebral damage was the Type 3 clinical course, characterized by slightly delayed postoperative recovery, followed by a period of normal behavior and then a lapse into stupor, terminated by coma and death. Recovery from stupor which developed after a postoperative period of normal behavior was not observed.

Minimum Mean Lethal Volume per Cent (MLV_{50}) of Acute Cerebral Damage in Untreated Animals.—All animals with less than 9.4 vol. % of cerebral damage survived, and all animals with more than 18.5 vol. % of cerebral damage died (Table 1). Of 49 animals with a quantity of cerebral damage in the range 9.4 to 18.5 vol. %, 29 survived and 20 died (Fig. 6). The average quantity of cerebral damage among the survivors was 13.7 vol. %, and that among the fatal cases was

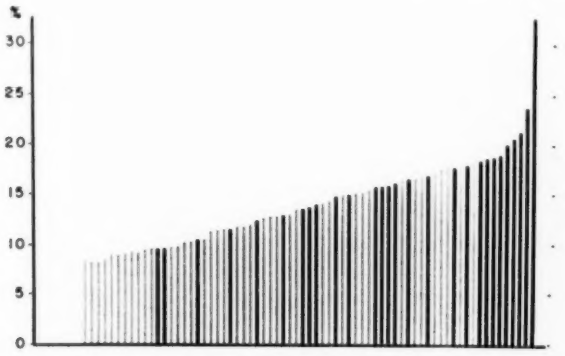

Fig. 6.—Each bar represents an animal with acute unilateral or bilateral cerebral lesions produced at one operation. The height of the bar indicates the volume per cent of cerebral damage. Each interrupted bar represents an animal that survived, and each solid bar, an animal that died. This graph, prepared from data in Table 1, does not include animals with 1.3 to 8.0 vol. % of cerebral damage.

14.9 vol. %. These values indicated that about half of a large group of animals with 14.3 vol. % of cerebral damage might be expected to survive. As this value is exceeded the probability of survival of any large series of animals should diminish rapidly to near zero at about 18.5 vol. % of cerebral damage. Hence, evaluation of usefulness of methods for reducing the mortality rate might best be carried out by studies of a large group of animals with about 14.3 vol. % of cerebral damage or a small group of animals with at least 18.5 vol. % of cerebral damage. With either method, quantitative data concerning the comparative benefits of different treatments might be obtained.

Value of Intravenous Administration of Hypertonic Dextrose Solution in Treatment of Acute Closed Cerebral Injury.—Six animals were given a single intravenous injection of a 10% aqueous solution of dextrose immediately after production of cerebral lesions (Table 2). The MLV_{50} of cerebral damage was 14.5 vol. %. This was of the same magnitude as the MLV_{50} of 14.3 vol. % in the untreated (control)

series. The maximum quantity of cerebral damage in a surviving animal was 16.9 vol. % of the brain. This was of the same magnitude as 18.0 vol. % in the untreated (control) series. It seemed that treatment of this type had little or no promise; so the experiment was terminated.

Two animals were given a single intravenous injection of 10% dextrose solution a short time after production of cerebral lesions (Table 2). Both died, with 12.8 and 16.8 vol. % of cerebral damage respectively. As indicated by data discussed in the previous paragraph, this method showed little promise and was dispensed with.

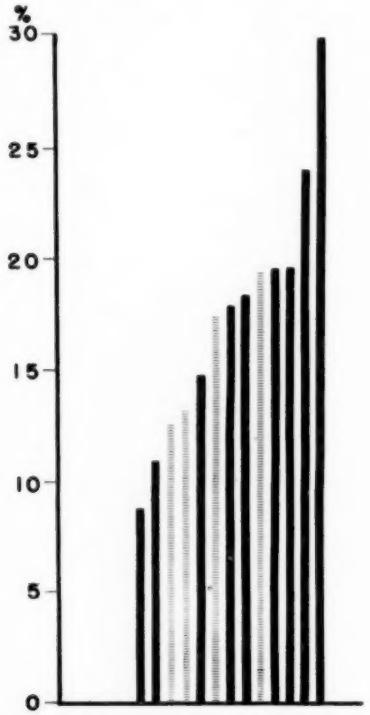

Fig. 7.—Each bar represents an animal given a continuous intravenous injection of a 25% aqueous solution of dextrose after production of a volume per cent of cerebral damage indicated by the height of the bar. The interrupted bars represent animals that survived, and the solid bars, animals that died.

Three animals were given a combination of immediate and delayed postoperative intravenous injections of 10% aqueous solutions of dextrose (Table 2). All died, with 14.7, 16.3, and 18.6 vol. % of cerebral damage respectively. As stated before, the results showed that the treatment had little promise, and it was not studied further.

Thirteen animals were given continuous intravenous injections of a 25% aqueous solution of dextrose. Dextrose administration was started immediately after production of cerebral lesions and continued at the rate of 6 to 8 ml. per hour until

the animal died or until complete recovery was apparent at the end of 24 hours (Table 2). Nine animals, with 8.9, 11.0, 14.9, 18.0, 18.4, 19.6, 19.7, 24.7, and 30.0 vol. % of cerebral damage respectively, died. Four animals, with 12.6, 13.3, 17.5, and 19,5 vol. % of cerebral damage respectively, survived. Calculations indicated that the MLV_{50} was about 14.5 vol. % of the brain (Fig. 7). The maximum quantity of cerebral damage in a surviving animal was 19.5 vol. %. Comparison of these data with those obtained for untreated animals showed that the treatment was of no significant value. It seemed that too much dextrose might have been given in some instances, but similar treatment of normal, intact animals had no adverse effect. Hence further plans to seek a more effective means of getting a beneficial result with intravenous injections of dextrose were given up.

Value of Surgical Decompression in Treatment of Acute Closed Cerebral Injury.—Removal of a bone flap on the side opposite the location of the cerebral lesion was done in four animals (Table 4). Three died, with 12.6, 13.5, and 15.2 vol. % of cerebral damage respectively. One survived, with 11.7 vol. % of cerebral damage. Since this operation seemed to decrease the chance of survival, no further experiments of this type were done.

Removal of a bone flap over each lesion within 30 to 45 minutes after production of lesions was done in 47 animals (Table 3). Some animals had unilateral lesions decompressed by removal of bone over the lesion. Others had bilateral lesions decompressed by removal of bone over both lesions. Small decompressions were dispensed with because preliminary studies indicated that they were relatively ineffective. Decompressions with an area greater than one-fourth to one-half the surface area of subjacent cortical lesions were usually difficult to do (Table 3). Among the 47 animals with decompressions, range in quantity of cerebral damage was 9.8 to 51.2 vol. % of the brain (Fig. 8). All animals with less than 14.6 vol. % of cerebral injury survived. This was considerably greater than 9.4 vol. %, the minimum lethal volume per cent of damage, in untreated (control) animals. The maximum survivable quantity of cerebral damage was 32.7 vol. % of the brain. This was also much greater than 18.0 vol. % in control, untreated animals. There were 35 animals with quantities of cerebral damage within the range of 14.6 to 32.7 vol. %. Seventeen animals survived, and 18 died. The MLV_{50} was about 21.9 vol. % of the brain (Fig. 8). This was about 50% greater than the MLV_{50} (14.3 vol. %) of control, untreated animals.

Removal of bone flaps was delayed until the onset of stupor or convulsions in eight animals (Table 4). These symptoms, indicative of a fatal lesion in control, untreated animals, developed within 45 minutes to 6 hours after production of lesions. Decompressions were then done, with removal of bone flaps over the lesions. Six animals survived, with 19.2, 19.4, 19.6, 21.5, 22.2, and 24.7 vol. % of cerebral damage respectively. Two animals died, with 21.0 and 49.4 vol. % of cerebral damage respectively. The average quantity of cerebral damage among the six surviving animals was 21.2 vol. %. This beneficial result was of about the same magnitude as that obtained by immediate postoperative decompression over the lesions.

Rate of Onset and Subsidence of Factors Responsible for Symptoms Following Production of Acute Closed Cerebral Lesions.—Successive cerebral lesions were produced at intervals of 24 hours in 12 animals, 48 hours in 12 animals, 72 hours in 4 animals, and 96 hours in 4 animals (Tables 5, 6, and 7).

In the group of 12 animals with lesions produced at intervals of 24 hours, the maximum survivable damage was 22.6 vol. %. The remaining 11 animals in this group behaved in the same manner as animals with comparable injury produced by multiple simultaneous lesions (Table 5).

The production of successive lesions at intervals of 48 hours led to survival of 5 of 12 animals, with 20.2 to 29.1 vol. % of cerebral injury. This was a clear indication that successive lesions had less effect when the interval between production of lesions was 48 rather than 24 hours (Table 6).

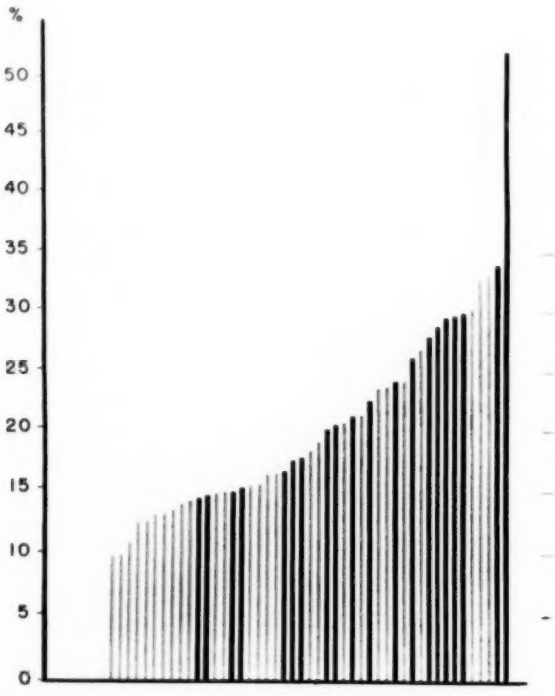

Fig. 8.—Each bar represents an animal with surgical decompression done within 30 to 45 minutes after production of a volume per cent of cerebral damage indicated by the height of the bar. The interrupted bars represent animals that survived, and the solid bars, animals that died.

Production of successive lesions at intervals of 72 hours led to survival of three of four animals, with 22.4, 23.6, and 25.9 vol. % of cerebral injury respectively (Table 7).

Production of successive lesions at intervals of 96 hours led to survival of the four animals, with 20.9, 26.8, 27.5, and 29.2 vol. % of cerebral damage respectively (Table 7).

These data show that the spacing of successive lesions at intervals of 24 hours had about the same effect on mortality as though the lesions had all been produced at one operation. When the interval between production of successive lesions was lengthened to 48 hours, animals were able to survive a greater volume per cent of

TABLE 5.—*Clinical Results of Increasing the Volume per Cent of Cerebral Damage by Production of Successive Cerebral Lesions at Intervals of Twenty-Four Hours**

Experiment No.	Volume per Cent of Brain Lesion				
	Lesion 1	Lesions 1 and 2	Lesions 1 to 3	Lesions 1 to 4	Lesions 1 to 5
83	6.8 (1)	13.7 (1)	22.6 (5)	25.1 (4)	.....
1	8.0 (1)	14.1 (2)	18.6 (2)	26.7 (4)	.....
84	8.9 (1)	12.1 (5)	16.4 (5)	20.8 (4)	.....
10	10.2 (1)	13.8 (5)	16.0 (4)	.....	.....
14	9.1 (1)	11.8 (4)	.....	.....	.....
16	1.3 (1)	8.1 (1)	15.2 (3)	.....	.....
15	4.2 (1)	4.6 (1)	5.9 (1)	7.9 (1)	8.1 (1)
8	7.9 (1)	15.5 (3)	.....	.....	.....
85	6.0 (1)	10.1 (3)	.....	.....	.....
86	5.7 (2)	11.1 (3)	.....	.....	.....
17	4.4 (1)	9.9 (3)	.....	.....	.....
6	4.2 (2)	7.1 (4)	.....	.....	.....

* The types of clinical courses are indicated by numerals (1-5) in parentheses adjacent to the volume per cent of cerebral damage.

TABLE 6.—*Clinical Results of Increasing Volume per Cent of Cerebral Damage by Production of Successive Cerebral Lesions at Intervals of Forty-Eight Hours**

Experiment No.	Volume per Cent of Brain Lesion					
	Lesion 1	Lesions 1 and 2	Lesions 1 to 3	Lesions 1 to 4	Lesions 1 to 5	Lesions 1 to 6
42	6.4 (1)	11.3 (2)	17.0 (1)	21.8 (5)	29.1 (5)	.....
43	4.5 (1)	11.0 (2)	17.3 (2)	25.5 (2)	29.0 (3)	.....
62	4.3 (1)	10.4 (1)	17.0 (2)	23.8 (5)	26.7 (3)	.....
60	3.8 (1)	7.3 (1)	14.7 (5)	18.3 (5)	21.7 (5)	21.9 (5)
67	4.2 (1)	11.0 (1)	15.9 (1)	20.2 (5)	28.2 (4)	.....
68	9.2 (1)	17.2 (1)	23.7 (3)	.....	.....	.....
61	7.0 (1)	16.9 (1)	23.0 (4)	.....	.....	.....
51	4.3 (1)	5.4 (1)	6.2 (1)	10.5 (1)	14.8 (5)	.....
30	7.9 (1)	9.8 (1)	13.4 (2)	.....	.....	.....
70	4.8 (1)	13.0 (1)	22.5 (3)	.....	.....	.....
59	11.2 (1)	15.5 (3)	.....	.....	.....	.....
21	4.4 (1)	9.3 (1)	13.9 (3)	.....	.....	.....

* The types of clinical courses are indicated by numerals (1-5) in parentheses adjacent to the volume per cent of cerebral damage.

TABLE 7.—*Clinical Results of Increasing the Volume per Cent of Cerebral Damage by Production of Successive Cerebral Lesions at Intervals of Seventy-Two Hours (Experiments 38, 20, 30, 37) and Ninety-Six Hours (Experiments 22, 41, 39, 40)**

Experiment No.	Volume per Cent of Brain Lesion					
	Lesion 1	Lesions 1 and 2	Lesions 1 to 3	Lesions 1 to 4	Lesions 1 to 5	Lesions 1 to 6
38	5.5 (1)	13.5 (3)	.....	.....	.....	.....
20	3.7 (1)	9.0 (1)	22.4 (5)	.....	.....	.....
30	5.0 (1)	10.9 (5)	16.7 (5)	23.6 (5)	.....	.....
37	7.3 (1)	15.2 (2)	18.2 (5)	19.6 (5)	22.3 (5)	25.9 (5)
22	8.1 (1)	13.5 (1)	15.1 (1)	16.9 (1)	20.9 (5)	.....
41	4.6 (1)	10.8 (1)	14.3 (1)	18.4 (1)	19.6 (1)	26.8 (1)
39	8.2 (1)	13.8 (1)	23.3 (5)	27.5 (5)	.....	.....
40	9.5 (1)	16.2 (1)	22.3 (5)	24.0 (5)	25.8 (5)	29.2 (5)

* The types of clinical courses are indicated by numerals (1-5) in parentheses adjacent to the volume per cent of cerebral damage.

cerebral damage. When the interval between production of successive lesions was still further lengthened to 72 and 96 hours, some additional advantage was gained, but this was not very great in terms either of survival or of recuperation of cerebral function. It seemed that factors responsible for lethal symptoms gradually increased in intensity for about 24 hours and gradually subsided, so that by the end of 48 hours their influence had largely disappeared. By taking advantage of this fact, it was possible to increase the survivable volume per cent of cerebral damage by 40 to 50%. The survivable magnitude of cerebral ablation was thereby extended to 50 vol. % of the cerebrum and to about 30 vol. % of the brain (Fig. 9). This could not be attributed to differences in size of successive lesions (Table 8).

The relations of the volume per cent of cerebral injury to the type of clinical course varied with the duration of the interval between production of successive

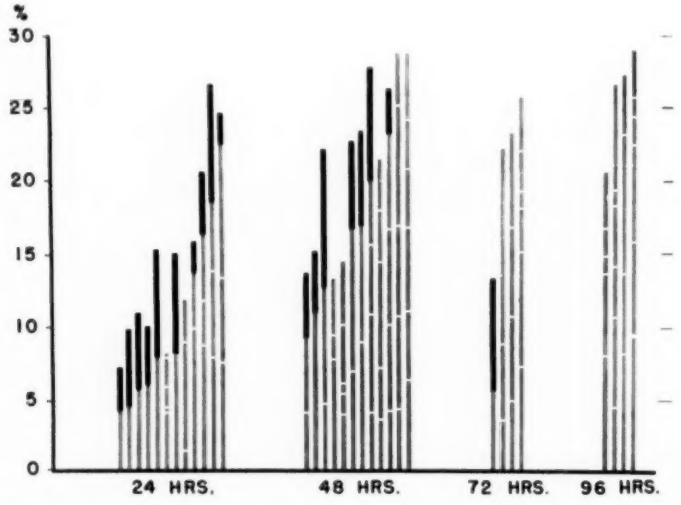

Fig. 9.—The total height of each bar indicates the sum of successive volume per cent of cerebral damage in an animal. Each bar is subdivided into columns which represent the individual volumes of each successive lesion. The time interval between production of successive lesions is indicated at the base of each group of bars. When the final lesion resulted in death, the volume per cent of the brain occupied by the final lesion is indicated by the length of the terminal solid section of the bar.

lesions. Data in Table 5 show that multiple lesions spaced at intervals of 24 hours led to essentially the same symptoms and clinical courses as lesions of similar volume per cent produced simultaneously. The only exception was that multiple spaced lesions were more frequently followed by a Type 5 clinical course in instances in which animals had a large total volume per cent of cerebral damage.

When successive lesions were spaced at intervals of 48, rather than 24 hours, the quantity of cerebral damage could, on the average, be increased 40 to 50% in representative surviving groups, such as those with Type 2 and Type 5 clinical courses. However, as the total volume of cerebral damage was progressively increased by increments at intervals of 48 hours, the animals tended to follow successively clinical courses in the sequence of Type 1 to Type 2 to Type 5 (Table 6).

When lesions were produced successively at intervals of 72 and 96 hours, the quantity of cerebral damage was still further increased with survival of the animal. The principal effect of the more prolonged interval between production of lesions, however, was to increase the number of animals surviving with Type 1 or Type 5 clinical courses and to decrease the number of animals following the fatal Type 3 and Type 4 clinical courses (Table 7). It seemed that this was due to a progressive reduction of total cerebral volume secondary to resorption of damaged cerebral tissue and to widespread cortical inactivation. In any event, there was more space within the cranium for expansion of the later acute lesions. Still further cerebral ablation could have been accomplished had the nutritional state of the animals been maintained during the semistuporous vegetative state of the Type 5 clinical course. Therefore, if extensive closed cerebral ablation is desired with minimum mortality, the interval between production of successive lesions should be at least 96 hours,

TABLE 8.—*Maximum, Minimum, and Average Volume per Cent of Brain Occupied by Lesions in Six Different Cerebral Locations in Four Groups of Experimental Animals with Multiple Lesions Spaced at Intervals of 24, 48, 72 and 96 Hours*

Time Interval Between Production of Lesions, Hr.	Size of Lesions	Volume per Cent of Brain					
		Lesion 1	Lesion 2	Lesion 3	Lesion 4	Lesion 5	Lesion 6
24	Maximum	10.2	7.6	8.9	8.1	...	...
	Minimum	1.3	0.2	1.3	2.0	...	...
	Average	6.4	5.4	4.6	4.5	...	...
48	Maximum	11.2	9.9	9.5	8.2	8.0	0.2
	Minimum	3.8	1.1	0.8	3.6	3.4	0.2
	Average	6.0	5.5	5.6	5.8	4.7	0.2
72	Maximum	7.3	8.0	13.4	6.9	2.7	3.6
	Minimum	3.7	5.3	3.0	1.4	2.7	3.6
	Average	5.4	6.8	7.4	4.1	2.7	3.6
96	Maximum	9.5	6.7	9.5	4.2	4.0	7.2
	Minimum	4.6	5.4	1.6	1.7	1.2	3.4
	Average	7.6	6.0	5.2	3.0	2.3	5.3

and artificial feeding should be instituted as soon as the apparently irreversible Type 5 clinical course becomes established.

COMMENT

Heretofore experimental studies of acutely expanding intracranial lesions have been conducted principally by traumatic methods. These methods introduce variables of concussion, cranial fracture, diffuseness of injury, or craniotomy, with their numerous complications. These variables have been largely eliminated or controlled by the method described in this report. Other variables, such as location, dimensions, and character of lesion, have only been partly controlled. There were limits as to location in which large volumes of damage could be conveniently produced. The most suitable locations were beneath those parts of the skull which were most accessible and least irregular or convex. For this reason, most lesions were produced in the superior convex parts of the cerebral hemispheres, extending in some cases from the tips of the frontal lobes to the tips of the occipital lobes. The technique was also limited in selective intracerebral inactivation. Discrete deep central cerebral lesions could not be produced without inactivating all overlying structures up to the surface of the cerebral cortex.

Dimensions of lesions of certain types were reproduced with reasonable accuracy in successive experiments. The range of error in reproduction of lesions with large or medium depth and breadth was no greater than ± 10% of the desired volumes. A greater error occurred when attempts were made to reproduce lesions of great diameter, small depth, and small volume. In general, the errors in reproduction increased with increasing divergence of values for diameter and depth.

The character of acute lesions was not constant. There was some variation in the type of necrosis, degree of hemorrhage, and amount of edema. In general, however, type and degree of necrosis were fairly uniform and always restricted to within sharply defined boundaries of the lesion. The amount of bleeding varied, but, again, this was restricted to within the boundaries of the lesion. There was no evidence of progressive bleeding into the lesion. The bulk of the hemorrhage occurred within a few minutes after production of the lesion, and thereafter there was spontaneous hemostasis. Variations in edema were difficult to measure. Edema varied within the lesion and in the adjacent portions of the cerebrum. It seemed to increase slowly during the first few postoperative hours and to be responsible for the frequently delayed onset of severe cerebral symptoms and death. Congestion, often of marked degree, was another variable which could not be suitably measured but which usually increased during the first few postoperative hours. Congestion and edema had largely subsided after 48 hours. Hemorrhage seemed unchanged. Necrosis was progressing, and resorption of degenerated tissue was beginning at this time. The resorption proceeded slowly, but early contraction of lesions and shrinkage of cerebral volume were apparent by the third or fourth postoperative day.

The discreteness and fairly uniform evolution and resorption of lesions greatly facilitated the quantitative studies which were made. In the first experiments, the relations of symptoms to the volume per cent of the brain occupied by acute lesions were defined. These studies showed that animals could tolerate at least 9.4 vol. % of cerebral damage without significant symptoms. When the quantity of cerebral injury was 9.4 to 18.5 vol. % of the brain, severe symptoms often developed. The mean minimum volume of cerebral damage lethal to 50% of animals was estimated to be about 14.3 vol. % of the brain, and the maximum survivable quantity of cerebral damage was 18.0 vol. % of the brain. The great majority of animals that died, even with more than 18.0 vol. % of cerebral damage, had a postoperative period of normal behavior which averaged three to four hours. Secondary lapse into stupor was a clear indication of impending coma and, except in rare instances, of eventual death within about 24 hours from the time of completion of the operation. These data indicated the feasibility of a quantitative experimental approach to the problem of treatment of acutely expanding closed intracerebral lesions, characterized by local necrosis, hemorrhage, and edema. The MLV_{50} and the maximum survivable volumes per cent of cerebral damage established the levels of magnitudes of damage necessary for defining benefits of treatment in terms of mortality. The postoperative delay in development of severe cerebral symptoms offered a period of sufficient duration to make possible the institution of various methods of treatment. The significance of these symptoms in terms of expected mortality permitted a still more critical evaluation of treatment when such treatment was delayed until the onset of symptoms known to indicate a lethal outcome in untreated animals.

With these facts in mind, experiments were carried out in an attempt to discover the best method of treatment with intravenous use of hypertonic dextrose solution.

No method of administration of dextrose, among the several used, had any effect upon either symptoms or mortality rate (Fig. 10). Had the experiments been more prolonged, the dextrose doubtless would have had nutritive value, but there was no evidence that it exerted any influence upon factors responsible for severe cerebral symptoms and death from cerebral causes.

Treatment of acute closed cerebral injury by surgical decompression was of real value if certain rules were followed in doing the decompression (Fig. 10). First, decompression was of little or no benefit unless it was done over the site of the lesion. Second, the area of bone removed in doing the decompression had to be at least one-fourth to one-half the submeningeal surface area of the lesion for satisfactory

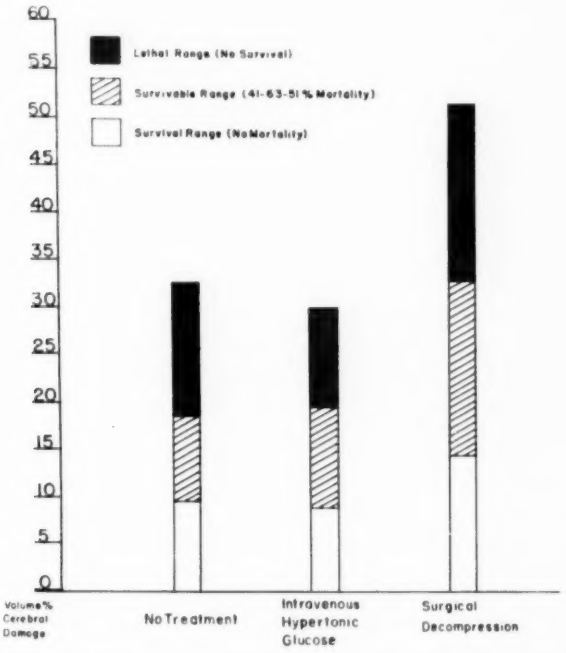

Fig. 10.—This graph compares experience gained in a study of three groups of animals with acute cerebral damage. One group was the large untreated series. The groups treated with intravenous administration of dextrose and surgical decompression over the sites of cerebral lesions are represented by the second and third bars.

benefit to be obtained. Third, although decompression shortly after production of lesions seemed more beneficial than delayed decompression, the difference was not very significant. When these rules were followed, severe cerebral symptoms were ameliorated in many animals, and the average amount of cerebral damage which could be tolerated with survival was increased about 50%.

An inquiry into the nature of factors responsible for symptoms was made by production of successive lesions at intervals of 24, 48, 72, and 96 hours. These studies showed that three variables were most important in governing the relations of the volume per cent of cerebral damage to clinical manifestations in animals. These

variables were, first, the volume per cent of acute cerebral damage; second, the volume per cent of cerebral damage due to previous injury, and, third, the interval of time which elapsed between production of acute damage and preceding injury. When successive sublethal lesions were produced at intervals of 24 hours, the effect was the same as if lesions had been produced simultaneously. When successive lesions were produced at intervals of 48, 72, or 96 hours, the mean survivable volume per cent of cerebral damage was greatly increased. The data indicated that a lapse of 48 hours after production of a near-lethal volume of cerebral injury was sufficient to permit the reproduction of a second near-lethal volume of cerebral injury, without death. Increasing the interval of time from 48 to 72 or 96 hours seemed to have a similar additional effect. These findings, together with the observation that the average life expectancy of animals with single acute lesions was about 7 hours, led to the conclusion that factors responsible for severe symptoms reached a maximum at about 7 to 10 hours after production of an acute lesion and that the factors persisted thereafter for at least 24 hours but disappeared rapidly in the interval between 24 and 48 hours after operation. Since these factors were combated by surgical decompression, and since there was no gross or microscopic evidence of progressive hemorrhage, it seemed that "toxic" substances could be largely disregarded in favor of space-occupying factors as causes of symptoms. Congestion and edema in and around the lesions were all that remained for serious consideration, and symptoms were therefore attributed to them. Although there was no complete proof that these were the factors, at least the curve of degree of influence of the factors in time was established.

By taking advantage of the subsiding influence of these factors, we could ablate large volumes of the cerebrum without opening the skull and without significant mortality by production of multiple, temporally spaced lesions. The survivable magnitude of cerebral ablation was about 50 vol. % of the cerebrum, or 30 vol. % of the brain. These values, theoretically, could be still further increased. However, as successive increments of cerebral damage were produced, the animals failed to recover normal behavior. They became lethargic and semistuporous and showed little ambition or desire to eat. The onset and persistence of these symptoms seemed to be more closely correlated with progressive subacute cerebral degeneration and widespread cortical inactivation than with total volume per cent of cerebral damage. We made no attempt to prolong life by artificial feeding. This would have been necessary had we desired to increase the amount of cerebral ablation with lesions produced, preferably, at intervals of 96 hours.

The possible application of the experimental observations to treatment of human intracerebral disease deserves comment. The use of a method employing low temperature for purposes of hemostasis in intracranial surgery should be investigated. There were reasons for gaining the impression that certain types of intracranial neoplastic tissue might be ablated successfully by killing tissue in situ by controlled local depression of its temperature, provided the neoplasm could be adequately approached. Emphasis may also be placed upon the advantage, at least experimentally, of multiple-stage ablation in giving time for congestion and edema of damaged cerebral tissue to subside between operations. There was no experimental indication that intravenous use of hypertonic dextrose solution was of any value in combating undesirable cerebral symptoms attributed to acute congestion and edema of the brain secondary to necrosis of tissue. It would seem that other methods aimed at reduction

of the congestion and edema should be developed. One method, already in common use, may deserve a broader application in attempting to relieve symptoms due to local acutely expanding intracranial lesions of either neoplastic or vascular origin. This is surgical decompression. It may be impractical or technically impossible to improve upon the current use of surgical decompression in these situations. If improvements are to be attempted, the experimental evidence indicates that certain rules might well be kept in mind. First, maximum benefits were obtained when decompressions were done over the lesions. Contralateral decompressions were of no value. Second, the value of decompression was roughly proportional to the size of the bone flap removed, so that satisfactory results were obtained only when the area of decompression was one-fourth to one-half the subarachnoidal surface area of the lesion. Third, although delay in decompression was not desirable, there was little significant difference in results of decompression before and after onset of symptoms due to otherwise lethal lesions. When these rules were followed, severe cerebral symptoms were ameliorated in many animals, and the average amount of cerebral damage which could be tolerated with survival was increased about 50%. Finally, it may be especially worth while to reevaluate surgical decompression as a method of treating selected patients with intracerebral vascular accidents. The prospective use of the method should be guided largely by the ability of the clinician to make an accurate anatomicopathologic diagnosis and prognosis before consideration of decompression as a life-saving measure.

SUMMARY AND CONCLUSIONS

Acute closed cerebral lesions were topographically and quantitatively reproduced in successive animals by local freezing of the cerebrum through the intact calvaria.

The lesions were discrete and characterized by a fairly constant degree of congestion, edema, hemorrhage, and necrosis.

The average minimum quantity of acute cerebral damage which was lethal to 50% of untreated animals was 14.3 vol. % of the brain.

The maximum survivable quantity of acute cerebral damage in untreated animals was 18.0 vol. % of the brain.

Correlations between symptoms and volume per cent of cerebral damage were fairly consistent. Most animals with lethal damage due to acute lesions had a postoperative period of normal behavior, lasting several hours. This was followed by onset of stupor, terminated by coma, convulsions, and death. Except in rare instances, the lapse into stupor was indicative of death within 25 hours of the time of completion of the operation.

Intravenous administration of hypertonic dextrose solution was of no value in reducing the severity of cerebral symptoms or the mortality rate due to acute closed cerebral injury.

Surgical decompression over the cerebral hemisphere opposite the location of cerebral lesions had no beneficial effect on the clinical course or the mortality rate.

Surgical decompression over each cerebral lesion was of definite value. Under appropriate conditions, cerebral symptoms were ameliorated, and the quantity of survivable cerebral damage was increased about 50%. These benefits were realized when the area of decompression approached one-half the subarachnoidal surface

area of the subjacent cerebral lesion. Decompression delayed until the onset of severe symptoms was of almost as great value as decompression immediately after production of lesions.

The volume per cent of cerebral damage which could be tolerated with survival was not increased by production of multiple successive cerebral lesions at intervals of 24 hours. However, when the interval between production of lesions was increased to 48, 72, or 96 hours, the survivable volume per cent of cerebral damage was increased to very large values. Limits of survivable damage were not defined because with additional small increments of damage animals regularly lapsed into an irreversible semistuporous state, with prospective death from inanition rather than from specific cerebral causes.

Factors responsible for acute cerebral symptoms and death from cerebral causes reached a maximum intensity 7 to 10 hours after production of lesions. Thereafter they persisted until about the 24th postoperative hour and thence declined rapidly, so that they seemed to have largely disappeared by the end of the 48th postoperative hour. It was concluded that congestion and edema, rather than toxic substances or progressive hemorrhage and necrosis, were the most important factors.

The combined results indicate that the mortality from certain types of human intracerebral disease might be reduced by application of principles evaluated here in quantitative terms.

AMYOTROPHIC LATERAL SCLEROSIS

A Clinicoanatomic Study of Fifty-Three Cases

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MODERN interest in amyotrophic lateral sclerosis stems from the pioneer publications of Duchenne [1] and Aran,[2] in which progressive spinal muscular atrophy was described and its muscular origin postulated. Opinion regarding the pathogenesis was divided thereafter between those who considered muscle and those who considered spinal cord the site of origin of the disorder. It remained for Charcot and Joffroy [3] to describe amyotrophic lateral sclerosis for the first time, and their classic papers gave overwhelming support to the neurogenic concept. In 1875 Erb [4] wrote about "a little-known spinal symptom complex," which since has been called primary lateral sclerosis. These conditions form the group known as "motor neuron disease," which also includes some special types characterized by aberrant age of onset (the progressive muscular atrophy of Werdnig and Hoffmann) or involvement of specific nuclei, such as Duchenne's progressive bulbar palsy. Motor neuron disease, therefore, may be manifested by amyotrophy alone or by pyramidal tract signs alone or, as was so ably presented by Charcot, by a combination of the two.

MATERIAL AND METHODS

The material utilized in the present study comprises 53 cases of amyotrophic lateral sclerosis and progressive spinal muscular atrophy with necropsy recorded in the files of the Montefiore Hospital for Chronic Diseases. There were no cases of a disease diagnosed anatomically as primary lateral sclerosis, and this problem, therefore, is not considered further. With one exception, only those cases were studied in which were available sections of the central nervous system from the motor cortex through the spinal cord. In all but seven cases a general necropsy had been performed. Thirty-three of the patients were males; 20 were females. The average

This study was aided by a grant from the Virginia Rosenthal Fund.

From the Laboratory Division and Division of Neuropsychiatry, Montefiore Hospital for Chronic Diseases.

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age of onset of the disorder was 48 years, with extremes ranging from 27 to 70 years. The duration of the illness varied from 3 months to 35 years, the average clinical course lasting 3.3 years (Table 1). The duration was usually similar regardless of the age of onset. Two patients had each a sibling with a similar disorder.

Weil's method of staining for myelin sheaths was utilized in the early cases; the techniques of Spielmeyer and Kultschitzky were used in later cases. Axis-cylinders were studied in Bielschowsky preparations. Sudan III and scarlet red were used to demonstrate fat. For the evaluation of gliosis, the Holzer technique was employed in some cases. Cell details were studied in preparations stained with cresyl violet or toluidine blue.

REPORT OF CASES

Eight cases have been selected for detailed report.

CASE 1.—T. P., a white man aged 32, noted onset of weakness and wasting of muscles of the left arm and hand in March, 1932, and one month later a similar affection of the left lower extremity. Four months later weakness and atrophy of the right lower extremity appeared, and then in two weeks there was a similar involvement of the right upper limb. In August dysphagia and dysarthria occurred. Physical examination revealed generalized weakness and atrophy of the skeletal muscles; fasciculation of the tongue and limb muscles; dysarthria; dysphagia, and generalized increase in deep reflexes, with Babinski and Hoffmann signs bilaterally. The hospital course, of 14 months, was characterized by gradual progression of

TABLE 1.—*Decade of Life at Onset and Duration of Disease*

Decade	No. Cases	Duration, in Years, in Individual Cases
20-29	2	3, 9
30-39	11	1, 1, 2, 2, 2, 3, 3, 4, 8, 9, 35*
40-49	12	1, 2, 2, 2, 2, 2, 2, 2, 2, 3, 5, 9
50-59	19	0.4, 0.5, 1, 1, 1, 1, 1, 2, 2, 2, 2, 2, 2, 3, 3, 3, 4*, 5, 5
60-69	8	1, 2, 2, 2, 2, 3, 3, 6
70-79	1	2

* The asterisk denotes the two cases of progressive spinal muscular atrophy.

disability, ending in death, due to aspiration pneumonia. Neuropathologic examination revealed severe and bilaterally equal involvement of the pyramidal tracts, the hypoglossal nuclei, and the ventral horn cells of the spinal cord. Cells of the nucleus ambiguus and dorsal motor nucleus of the vagus nerve were minimally altered.

Comment.—This case illustrates a typical course of amyotrophic lateral sclerosis.

CASE 2.—J. F., a white woman aged 36, from 1928 to 1931 had "stiffness" and weakness of the right lower extremity and then noted gradual weakness of the right upper limb. Examination on her admission to the hospital five years after onset of the illness revealed a hemiplegic gait, but there were bilateral pyramidal tract signs, with predominance on the right. In 1934 her left leg became weak. Hypertonicity of the left arm and fasciculations in the tongue were noted in 1936. Difficulty in swallowing then occurred, and she died, in respiratory failure, in 1937, nine years after onset of the illness.

Comment.—This and the following two cases are instances of amyotrophic lateral sclerosis which clinically are less common. The patients had asymmetric pareses for relatively long periods. Case 2 is unusual because of the initial hemiplegia and the slow progression to typical amyotrophic lateral sclerosis.

CASE 3.—J. M., a white man aged 40, noted in the summer of 1941 the onset of weakness of the left lower extremity, with progression to paralysis one year later. Not until January, 1944, did weakness of the left upper extremity manifest itself. Soon afterward the right lower extremity became weak, and then the right arm was affected. In July, 1944, there were bulbar signs. The patient died 40 months after the onset of his ailment.

Comment.—Almost three years elapsed between the onset of weakness of one extremity and the appearance of clear-cut signs of amyotrophic lateral sclerosis. The diagnosis obviously was difficult until there were signs of fulminant progression.

CASE 4.—A. S., a white man aged 50, became aware of paresis of the muscles of the right leg in May, 1943. Eleven months later the left lower extremity became weak. Thereafter both arms became weak, and in May, 1944, there was difficulty in talking and swallowing. The total duration of the disorder was 26 months.

Comment.—This case illustrates a transition between the more typical Case 1 and the atypical Cases 2 and 3.

CASE 5.—E. H., a white woman aged 45, suffered the onset in March, 1944, of continuous sharp "shooting" pains in the right leg, with ensuing weakness. During the subsequent three months pains of comparable character occurred in the left leg and right arm, which also became weak. Some months later the left arm was similarly affected. Weakness of trunk muscles, a change in speech, and dysphagia followed. The power of the limb muscles diminished progressively. Examination revealed weakness and atrophy of most muscle groups, the changes being more prominent distally and greater on the right than on the left; fasciculation of muscles of the tongue, hands, and thighs; spasticity of all four limbs; active abdominal reflexes, and generalized hyperreflexia, with a Babinski sign bilaterally and clonus of the right ankle. The hospital course, of 11 months' duration, was characterized by gradual progression of bulbospinal signs and death, from bronchopneumonia. Neuropathologic examination revealed severe demyelination of the pyramidal tract from the internal capsule through the lumbar portion of the spinal cord and diffuse alterations of cells in the motor cortex, the hypoglossal nucleus, the nucleus ambiguus, and the ventral horns of the spinal cord.

Comment.—The initial sensory complaints in this case are of interest. Subjective complaints of sensory phenomena occurred in a total of six cases, but anatomic examination of the sensory pathways gave entirely normal findings in all but Case 6.

CASE 6.—R. Z.,[5] a white woman aged 56, fell in March, 1929, striking her right shoulder. Severe local pain ensued, which was episodic. Three months later pain in all extremities was noted. Soon thereafter she complained of weakness and of atrophy of the muscles of the upper limbs and of stiffness of the lower limbs. Examination revealed definite paresis of the upper extremities, especially the hands; marked spasticity of the lower limbs; active deep reflexes; absence of abdominal skin reflexes; Hoffmann and Babinski signs bilaterally; atrophy of muscles of the hands and forearms; fasciculations of the tongue, arm, shoulder, and thigh muscles, and loss of vibratory sensation in the lower extremities, but no other disturbances of sensation. The course of seven months' duration, was characterized by progression of signs, with development of bulbar paralysis and death in respiratory failure. Neuropathologic examination revealed diffuse motor cell degeneration from the cerebral cortex through the spinal cord, demyelination of the pyramidal tract from the internal capsule through the lumbar portion of the spinal cord, and demyelination of the fasciculus gracilis in the cervical and thoracic sections of the spinal cord with well-defined gliosis (Fig. 1).

Comment.—The anatomic demonstration of sensory fiber demyelination in this case is unique in the series. The demyelination may be considered either as a coincidental finding or as an unusual variant of amyotrophic lateral sclerosis. Our interpretation is the former. This assumption is based on the diffuse, nonsystematic alteration of the lower thoracic region of the spinal cord, with secondary ascending

5. This case has been reported in another publication (Wechsler, I. S., and Davison, C.: Amyotrophic Lateral Sclerosis with Involvement of Posterior Column and Sensory Disturbances, Arch. Neurol. & Psychiat. **35**:229-239, 1936).

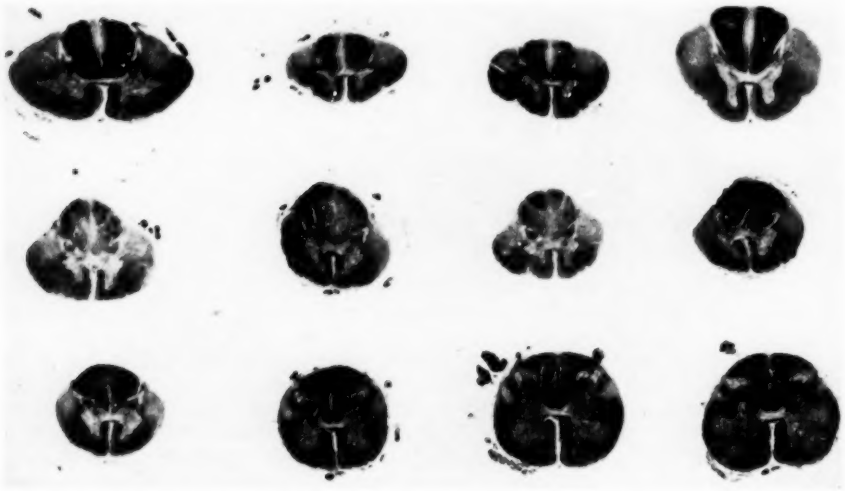

Fig. 1.—Multiple sections at various levels of the spinal cord. In the thoracic group (middle row) widespread transverse demyelination is present. All sections above these levels reveal ascending demyelination, involving chiefly the fasciculus gracilis. Lateral column demyelination is present at all levels. Weil stain; × 2.5.

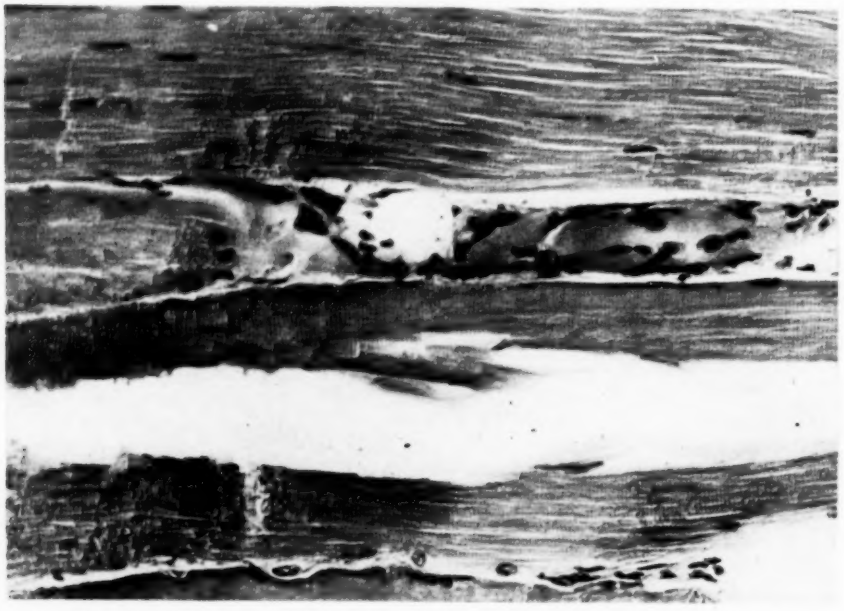

Fig. 2.—Dystrophic changes within fibers of the anterior tibial muscle in a case of amyotrophic lateral sclerosis. The uppermost fiber is wider than normal. The fiber below contains a focal proliferation of sarcolemmal nuclei and zones of loss of muscle substance. Cross striations are lost irregularly in this fiber but are normal in the other fibers. Hematoxylin-eosin stain; × 250.

demyelination. The cause of the damage in the thoracic segments was not determined, but because of onset with a fall a traumatic origin may be suggested. There are no other known instances of amyotrophic lateral sclerosis with such segmental disorder.

CASE 7.—G. B., a white woman aged 54, had onset of weakness in the right lower extremity in January, 1938. One year later there was pain in the right leg in walking. In 1940 weakness and pain occurred in the left leg. Subsequently gradual "thinning" of the legs and increasing difficulty in walking were noted. Physical examination revealed paraparesis with bilateral foot drop; flexion contractures of the toes; absence of fasciculations; steppage gait; absence of deep reflexes in the lower extremities; absence of abdominal skin reflexes, and absence of pathologic reflexes or sensory disturbances. In August, 1942, the patient complained of pains in the hands similar to those experienced in the feet. Objective weakness of the upper extremities was not found, but the patient died suddenly in November, with pulmonary emboli. Neuropathologic examination revealed striking loss of ventral horn cells in the lumbar, thoracic, and cervical regions of the spinal cord. There was no pyramidal tract demyelination. Examination of the muscles of the lower extremities revealed atrophy of motor units, but, in addition, there were definite dystrophic changes within nonatrophic muscle fibers (Fig. 2).

Comment.—This case is one of progressive spinal muscular atrophy. It took the form of a paraplegia, although there were subjective signs of changes in the upper extremities, and anatomically the anterior horn cells in the cervical region were characteristically altered. The surprising findings, however, were those of a primary disorder of muscles. This combination is indeed rare, and is considered further in the discussion.

CASE 8.—F. C., a white man aged 72, noted the onset of weakness of the muscles of both hands at the age of 37. During the next 35 years paresis and atrophy of the muscles of both upper extremities and shoulders developed. In November, 1948, the patient began to suffer from pain in the lower part of the back, with radiation down the posterior aspect of each lower limb. Two weeks later melena occurred. Physical examination revealed a pulsating abdominal mass; mental obtundity; atrophy, fasciculation, and weakness of the muscles of both shoulders and upper extremities; absence of deep reflexes in the right upper limb; absence of abdominal skin reflexes, and a Babinski sign on the right. During the following 16 months the only change in neurologic status was the appearance of a Babinski sign on the left. The patient died with acute hepatitis after a blood transfusion. Necropsy revealed jaundice, splenomegaly, ascites, acute centrilobular necrosis of the liver, generalized arteriosclerosis, an aneurysm of the abdominal aorta, and a chronic duodenal ulcer. Neuropathologic examination revealed a moderate degree of gyral atrophy, most marked in the left frontal region; generalized shrinkage of the spinal cord, and demyelination of the lateral pyramidal tracts. There were moderate diminution in number and alteration of Betz cells and of ventral horn cells in the lumbar region of the spinal cord. At the thoracic and cervical levels of the spinal cord almost no ventral horn cells were seen, and cell details were altered in the few cells remaining. There was demyelination of pyramidal tract pathways from the internal capsule through the lumbar portion of the spinal cord.

Comment.—The 35-year course of the disease in this case is notable and unique in the present series. Most interesting were the presence of fasciculations in the muscles of the upper limbs and shoulders so long after the onset of the illness and the late development of the Babinski sign. There is a clear indication that this case of slowly developing progressive spinal muscular atrophy became one of amyotrophic lateral sclerosis, both clinically and anatomically. There were no anatomic differences between this form of amyotrophic lateral sclerosis and the forms of characteristic brief duration. Such a case offers valuable evidence of the validity of the concept of "motor neuron disease" by showing the transition from one disorder to another.

ANATOMIC OBSERVATIONS

Most of the earlier cases were collected by Dr. Charles Davison. Some of these cases have been reported in previous communications by Dr. Davison and others [6]; in certain instances our evaluation of the material has resulted in a revised interpretation.

Associated anatomic findings in the 46 cases with complete necropsy included generalized arteriosclerosis, 14 cases; thyroid adenoma, 4 cases; abdominal aortic aneurysm, 2 cases; trichinosis, 1 case; chronic duodenal ulcer, 1 case, and carcinoma of the sigmoid colon, 1 case.

Death in most instances was associated with infections of the respiratory tract. In 25 cases bronchopneumonia was found at necropsy; in 14 others "respiratory failure" was noted clinically and in 3 cases pulmonary infarction was present. In one case death was the result of a cerebral hemorrhage, and in one (Case 8) death from hepatitis followed a transfusion. In nine cases the cause of death was not determined.

Brain weights ranged from 1,150 to 1,650 gm., with an average weight of 1,400 gm. The gross appearance of the brain was abnormal in 27 cases and normal in 24;

TABLE. 2—*Severity of Involvement of Cells and Myelin Sheaths in Fifty-Three Cases*

	No. of Cases		
Severity	Betz Cells	Ventral Horn Cells	Myelin Sheaths
—	0	0	2
+	5	1	4
++	11	8	11
+++	16	20	9
++++	17	24	27
Total.....	49*	53	53

* In four cases preparations of the motor cortex were not available or the motor cortex could not be identified.

a description was lacking in 2. Of the abnormal group, gyral atrophy in the frontal region was noted in 13. In 11 cases there were grossly visible changes in the brain stem, i. e., shrinkage of the cerebral peduncles, generalized decrease in size of the pons or medulla, chalkiness, and diminution in size of the pyramids. Mild to moderate ventricular dilatation was noted in eight cases.

Gross alterations were observed more frequently and more consistently in the spinal cord than in the brain, being represented in 29 cases by a chalky appearance of the lateral pyramidal tracts. In 6 cases the spinal cord was described as grossly normal, and in the remainder generalized atrophy was noted or a macroscopic description of the cord was not available.

An attempt was made roughly to grade the degree of histologic alteration of the nerve cells and their processes, an arbitrary scale of — to ++++ being employed

6. (*a*) Wechsler, I. S., and Davison, C.: Amyotrophic Lateral Sclerosis with Involvement of Posterior Column and Sensory Disturbances, Arch. Neurol. & Psychiat. **35**:229-239, 1936; (*b*) Amyotrophic Lateral Sclerosis with Mental Symptoms: Clinicopathologic Study, ibid. **27**:859-880, 1932. (*c*) Davison, C.: Effect of Vitamin E Therapy on the Central Nervous System in Amyotrophic Lateral Sclerosis, Am. J. Path. **19**:833-899, 1943; (*d*) Amyotrophic Lateral Sclerosis: Origin and Extent of the Upper Motor Neuron Lesion, Arch. Neurol. & Psychiat. **46**:1039-1056, 1941.

for this purpose. The degree of demyelination of the pyramidal tracts and the severity of the involvement of Betz cells and ventral horn cells are summarized in Table 2. Individual cases varied greatly in degree of cellular and myelin sheath alteration. The only universal finding in cases in which suitable preparations were available was at least some alteration of Betz cells and ventral horn cells.

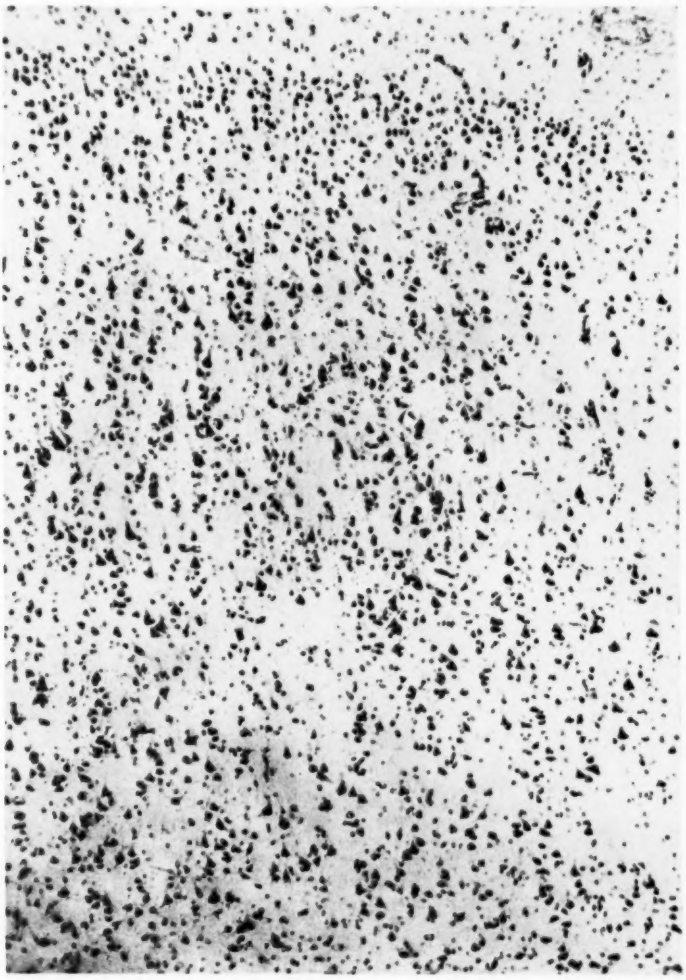

Fig. 3.—Small foci of cell loss scattered in the motor cortex. Many cells are pale. There are no large cells of Betz. Nissl stain; × 75.

Preparations of the cerebral cortex included the motor area in almost all instances, and adjacent cortical tissue as well. One of the most striking features of this portion of the study was the diminution in numbers of Betz cells in all cases (Table 2) and their almost complete absence in many (Fig. 3). Cell changes of

various types, i. e., chromatolysis, vacuolation of cytoplasm, nuclear eccentration or loss, shrinkage of cell body, axonal change, and satellitosis, were prominent (Fig. 4*A*). In addition to these cellular alterations in the fifth layer of the motor

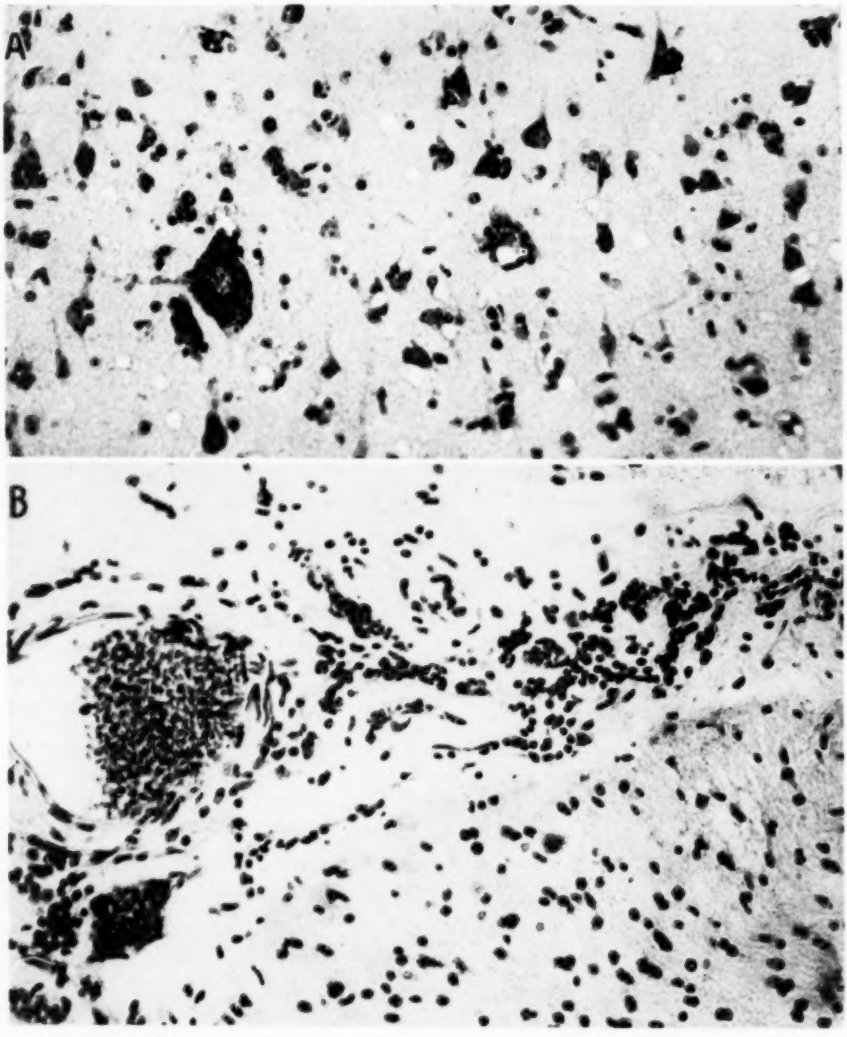

Fig. 4.—*A*, high-power view of the fifth cortical layer of the motor area. At the far left is a glial nodule. A single intact Betz cell is present in the center. To the right a large neuron has a vacuolated cytoplasm and many satellites. Nissl stain; × 250.

B, a small number of lymphocytes in the perivascular space of a blood vessel in the white matter. Nissl stain; × 200.

cortex, cellular changes were noted in other layers in many cases. Loss of small pyramidal cells and microscopic cortical lacunae frequently was observed, as well as distinct glial proliferation of various degrees. Of further interest were the foci

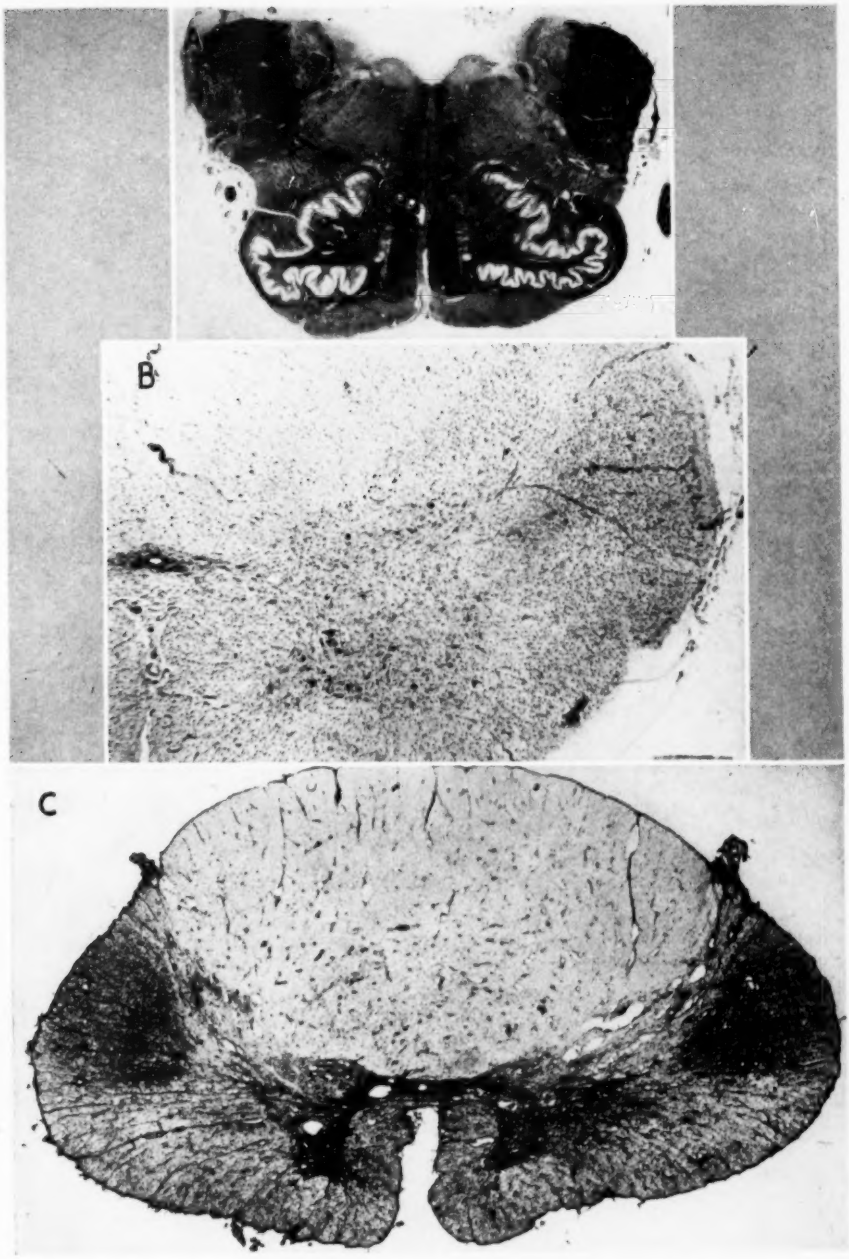

Fig. 5.—*A*, section through the medulla at the level of the olivary nuclei. The pyramids are strikingly smaller than usual, demyelinated, and lacking in the usual ventral protrusion. The remainder of the medulla is intact. Kultschitzky's myelin stain; × 5.5.

B, section through the lumbar region of the spinal cord. The number of glial cells in the anterolateral columns is increased as compared with that in the posterior columns. The condensation and reactive gliosis are most prominent in the region of the lateral pyramidal tract. Nissl stain; × 45.

C, gliosis of the anterolateral funiculi, most prominent in the lateral pyramidal tracts. Holzer stain; × 24.

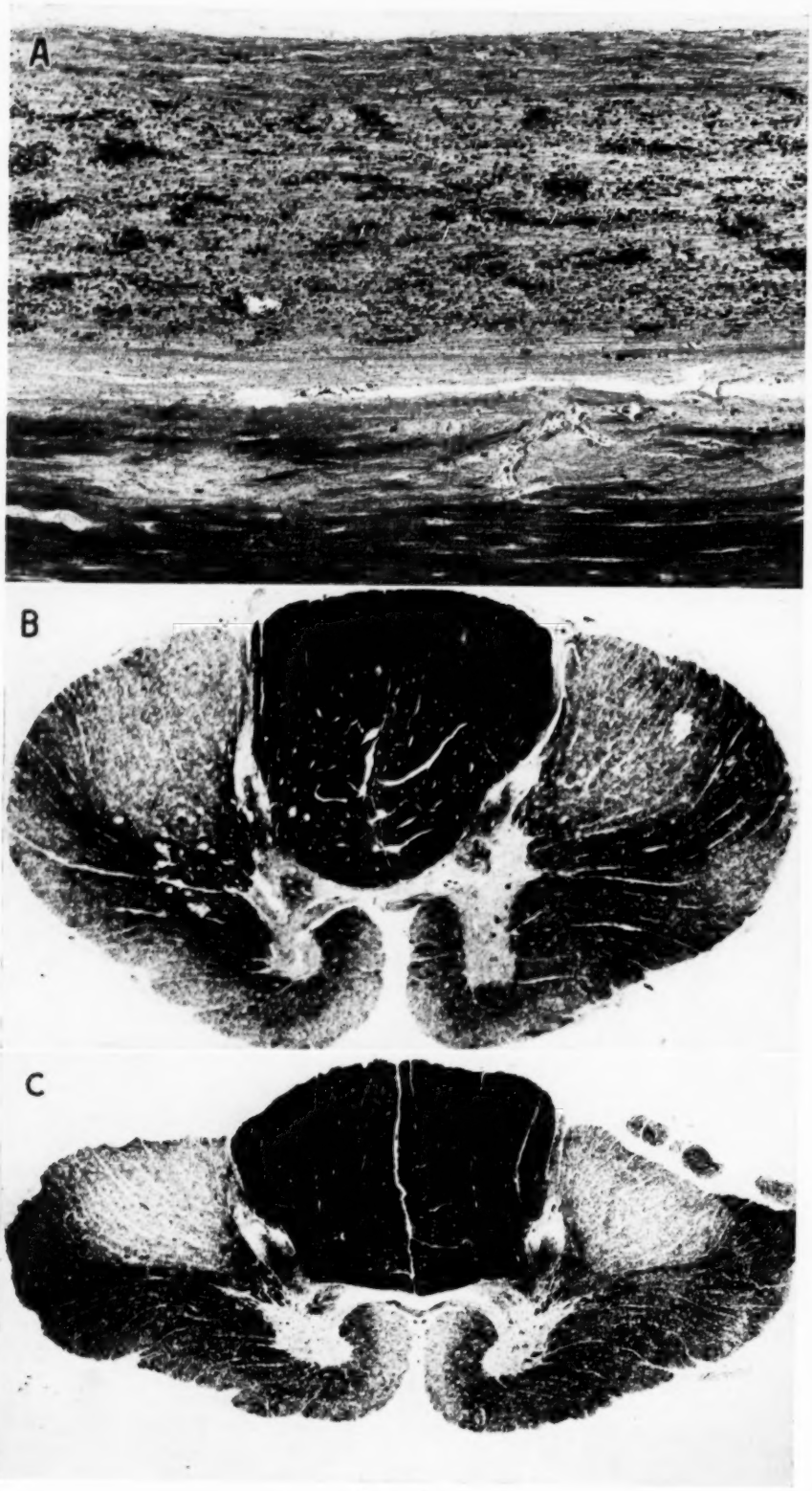

Figure 6

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of loss of cortical cells or cellular alteration in the granular cortex adjacent to Area 4. In a number of instances the motor cortex was noticeably thinner than usual. In these cases, indeed, it was not until the agranular character of the cortex had been recognized and a few Betz cells seen that identification could be made with certainty.

Small perivascular lymphocytic accumulations were present in the gray or the white matter (Fig. 4 *B*) in some cases.

In all but two cases alteration of myelin sheaths of various degrees was revealed. It is of paramount importance that a demyelination of the pyramidal tracts from the internal capsule through the spinal cord was noted in 51 cases. Myelin changes consisted of shrinkage, ballooning, bubbling, and vacuolation of sheaths, as well as a definite decrease in numbers of sheaths in some instances. Demyelination of medullary pyramidal tract fibers was accompanied in some cases by flattening and shrinkage of the pyramids (Fig. 5*A*). In certain instances the degree of myelin loss or alteration in the pyramidal tracts was severer and the gliosis more noticeable in the brain stem than in the spinal cord, although the reverse usually was true.

Reactive and "condensation" gliosis was of great aid in confirming alteration of myelin. Preparations stained by Nissl's method (Fig. 5 *B*), as well as by Holzer's technique (Fig. 5 *C*), occasionally showed more striking evidence of pathologic change than was evidenced with the myelin sheath stain. Additional confirmation was obtained by use of material stained for fat, free lipid being noted in the demyelinated areas (Fig. 6*A*).

We were struck by the widespread involvement of fibers in the anterolateral funiculi of the spinal cord in most instances (Fig. 6 *B*). The sheath changes, glial "condensation" and proliferation, and fat deposition were most evident in the region commonly regarded as the site of the lateral pyramidal tract (Fig. 6 *C*). Minimal changes in sheaths, as well as accompanying gliosis and globules of free fat, were not unusual in other portions of the anterolateral funiculi. In most cases myelin sheath changes were prominent in the fiber network of the anterior horns of the spinal cord. Many sheaths of the ventral root fibers were ballooned and distorted within the substance of the spinal cord; the extraspinal portions, however, usually were normal in appearance. Demyelination of the anterolateral columns was symmetric in the majority of cases. The lateral pyramidal tracts were altered somewhat asymmetrically in only five cases (Fig. 7*A*).

The changes in myelin sheaths of the anterior corticospinal tracts, on the other hand, were more frequently unequal on the two sides, an asymmetry being found in 17 cases (Fig. 7 *B*). The lateral corticospinal pathways were involved alone in eight instances. A common variation was found in the contour of the anterior corticospinal

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EXPLANATION OF FIGURE 6

Fig. 6.—*A*, longitudinal section in the lumbar region of the spinal cord. Numerous fat granules are scattered among the fibers of the lateral pyramidal tract on the left. Many fat granules are concentrated around blood vessels. The medial pathways on the right are free from fat. Sudan III technique; × 25.

B, widespread demeylination of the anterolateral columns. The posterior columns stand out prominently by contrast. Weil stain; ×16.5.

C, generalized demyelination of the anterolateral column with greatest prominence in the crossed and uncrossed pyramidal tracts. Weil stain; × 21.

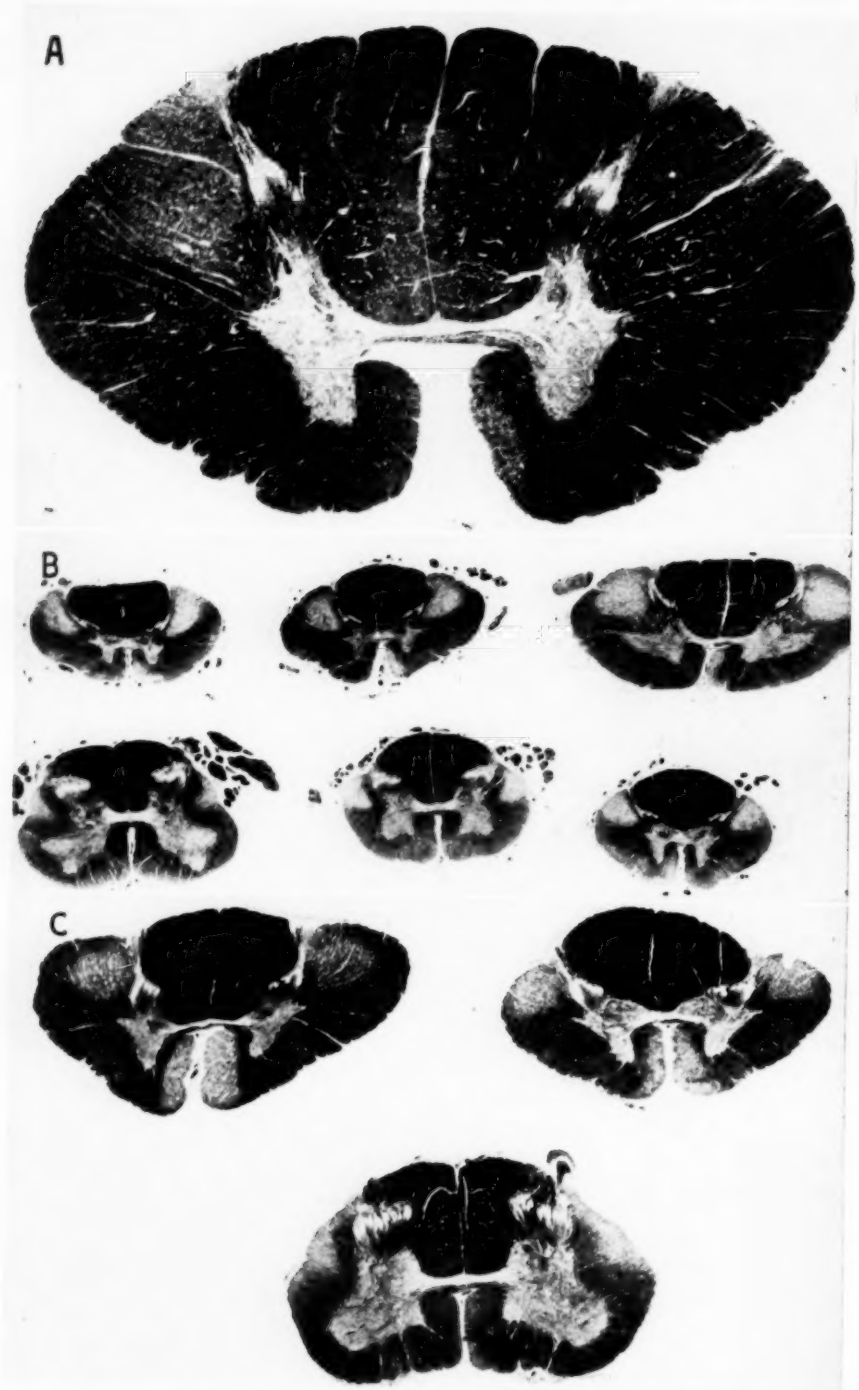

Fig. 7.—*A*, asymmetric demyelination of the crossed and uncrossed pyramidal tracts. On microscopic examination, both sides were seen to be affected. The macroscopic examination overemphasized the mild asymmetry. Spielmeyer stain; × 13.

B, asymmetric demyelination of the ventral (uncrossed) corticospinal tract, although the demyelination of the lateral (crossed) tract is similar on the two sides. Note the comma-shaped demyelination at one level. Weil stain; × 4.3.

C, variation in the type of demyelination of the pyramidal tracts. In this case the area of demyelination in the uncrossed tract is larger than is usually encountered and is comma-shaped in the thoracic region. Weil stain; × 9.

tract in the cervical and thoracic regions of the spinal cord. This is shown in Figure 7 *B* and *C*. Surprisingly, in one instance fibers in this location were demyelinated in the lumbar region. Despite these minor variations, it should be emphasized that the demyelination was predominantly systematic and symmetric (Figs. 6 *B* and *C*, and 7).

In one case definite demyelination, although incomplete, of the fasciculus gracilis was found in the thoracic and cervical regions of the spinal cord, in addition to involvement of the motor system (Case 6). This was the only case in which definite anatomic evidence of sensory-tract alteration was found.

Involvement of the cranial nerve nuclei was in a definite pattern. In 50 cases in which appropriate sections were available, cells of the hypoglossal nuclei were affected. The cell changes varied from almost complete destruction of nuclear components to minimal dropping out of cells, with mild changes in the elements of those remaining (Fig. 8*A*). In a few cases the hypoglossal nuclei were asymmetrically altered.

Alteration of cells of the nucleus ambiguus was noted in 43 instances, and these changes varied from complete destruction, in two instances, to minimal cell changes. As with the nuclei of the 12th nerve, asymmetric involvement occurred rarely. In 35 patients cellular loss or degenerative change was noted in the dorsal motor nuclei of the vagus nerves.

Preparations of the medulla stained by Nissl's technique showed definite cell deterioration in the external arcuate nuclei in two cases. In four instances cell changes of different severity were found bilaterally in the motor nuclei of the trigeminal nerve. In four cases cells of the oculomotor nucleus were altered.

It is noteworthy that there was some alteration of ventral horn cells in all sections of the spinal cord (Fig. 8 *B*, *C*). Evidences of cellular degeneration included satellitosis, pyknosis, and eccentration of the nucleus; loss of chromatin; shrinkage of the cell body, and axonal change (Fig. 9 *A*, *B*). Some cells consisted of a thin membrane with dendritic processes enclosing a faintly stained amorphous material. Neuronophagia was distinguished by its rarity.

Agonal hemorrhages were prominent in the gray and, to a less extent, the white matter of the spinal cord in many preparations (Fig. 9 *C*). In some cases the hemorrhages were extensive—in one an entire ventral horn was replaced by fresh blood. Perivascular lymphocytic infiltration was not uncommon in the central gray matter, less common in the adjacent white matter.

Peripheral nerves were available in only a few cases, and the myelin sheaths and axons were normal in all.

Sections of skeletal muscle revealed atrophy of motor units in all available cases (Fig. 10) save one, in which definite dystrophic changes were seen (Case 7, Fig. 2). Study of skeletal muscle is of value in determining the nature of the disorder in cases of this disease, especially when the differential diagnosis includes consideration of a myopathy. The alterations of muscle in amyotrophic lateral sclerosis usually can be distinguished from those occurring in primary muscle disorders. The principal feature in amyotrophic lateral sclerosis is the distribution of the altered fibers. Motor units are affected, resulting in a characteristic picture—groups of atrophic fibers separated by clusters of normal fibers. The affected fibers are altered along

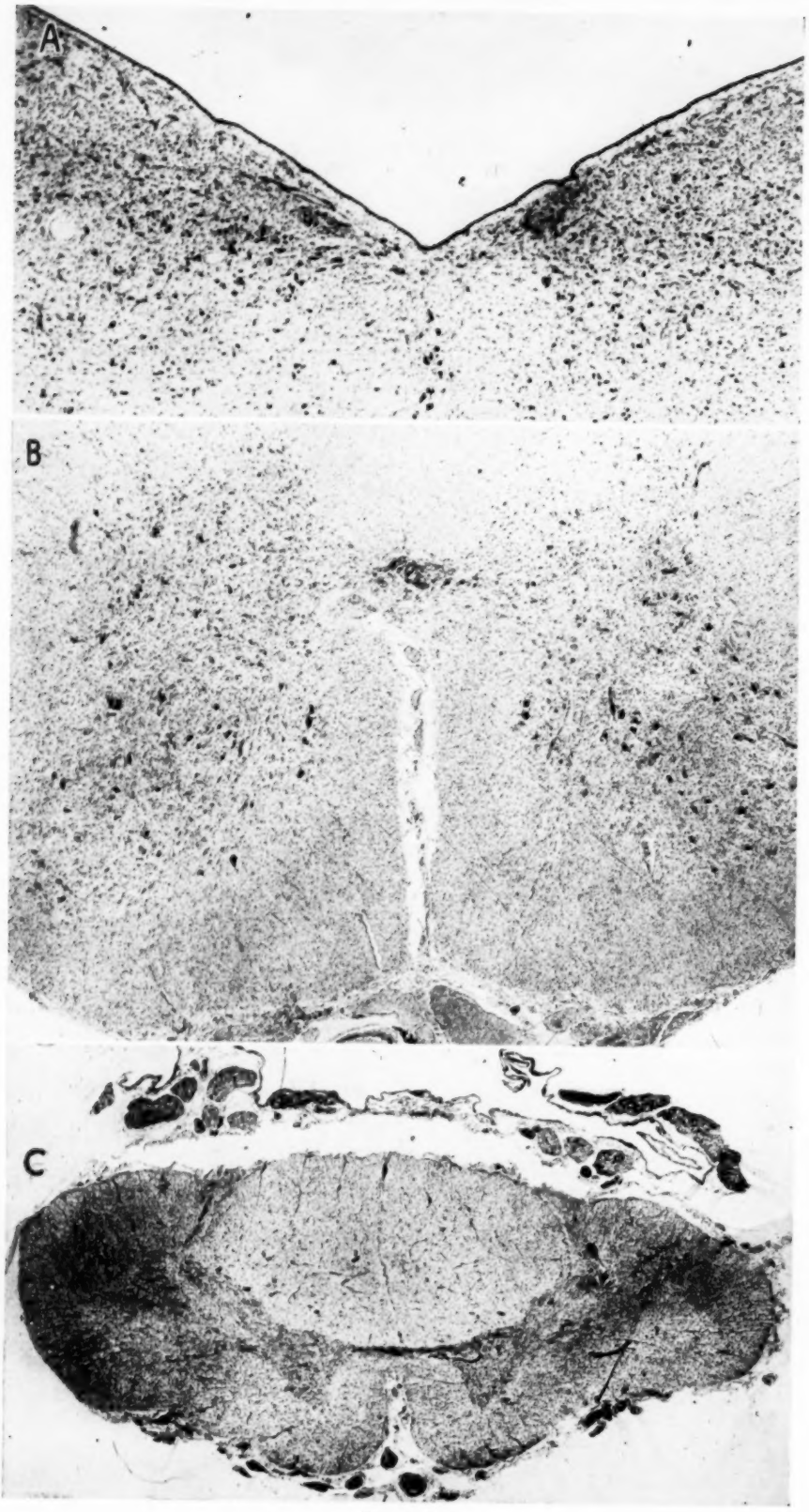

Figure 8

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their entire length. They are oftenest reduced in width, and there is frequent loss of the recognizable features of striated muscle. The sarcolemmal nuclei are increased in number, usually, however, at the edges of fibers. Muscle fibers may be replaced by connective tissue. Fatty tissue infiltration, often described as a distinguishing feature of muscular dystrophy, also may occur in secondarily atrophic muscles (Fig. 10*A*). The distinguishing features of muscular dystrophy need not be mentioned except to indicate that the distribution of the lesions is different—the lesions are focal and within muscle fibers (Fig. 2). The major difficulties in diagnosis are encountered in the late stages of atrophy and dystrophy, when differentiation may not be possible.

CLINICAL OBSERVATIONS

Onset of the clinical disorder was characterized by bulbar signs in 14 cases. Of these, the initial complaint was of dysphagia in 4 and of speech impairment in 10. Of the remaining 39 cases, neurologic signs first were noted in the lower extremities in 24 (see "Comment"), in the abdominal musculature in 1, and in the shoulders or upper extremities in 14. Fasciculations were present in 52 cases at some time during the illness. In 10 cases forced laughing or crying was noted. It is of interest that premonitory complaints of a sensory character were recognized by six of the patients. Four noted cramp-like pain, and one, a lancinating pain affecting one lower extremity, and in one a sensation of coldness preceded by months the onset of motor signs in the involved extremity.

In 38 of the 53 cases generalized muscular wasting was noted; in 10 atrophy was limited to the upper extremities and shoulder girdle, and in 2 muscular atrophy was confined to the lower limbs. In only one case was asymmetric atrophy of the intrinsic muscles of the hand noted initially and maintained throughout the course of the patient's illness. This was the only case in which such inequality was apparent at all times. Symmetric muscular atrophy is one of the distinguishing features of amyotrophic lateral sclerosis, although in some instances it may not be evident for months, or rarely for years. Asymmetric motor deficits were noted in five cases for relatively long periods, of more than a year. These are exemplified in Cases 2, 3, and 4.

The clinical course was progressive in 50 cases. In hospital records of the remaining three cases note was made of temporary improvement at some time during the illness, but in each case the reference was vague.

Laboratory procedures, i. e., urinalyses, blood counts, and determinations of blood chemistry values, were within normal limits, or deviations could be explained

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EXPLANATION OF FIGURE 8

Fig. 8.—*A*, section from the floor of the fourth ventricle through the hypoglossal nuclei. The hypoglossal cells are diminished in number, and the remaining neurons are strikingly shrunken. The dorsal motor nucleus of the vagus is similarly altered. Nissl stain; × 35.

B, lumbar region of the spinal cord. There is loss of anterior horn cells, which is more striking on the left side. Nissl stain; × 30.

C, only a few small remaining neurons in the shrunken anterior horns at the cervical level of the spinal cord; gliosis in the anterolateral funiculus, most prominent in the lateral pyramidal tracts. Nissl stain; × 23.

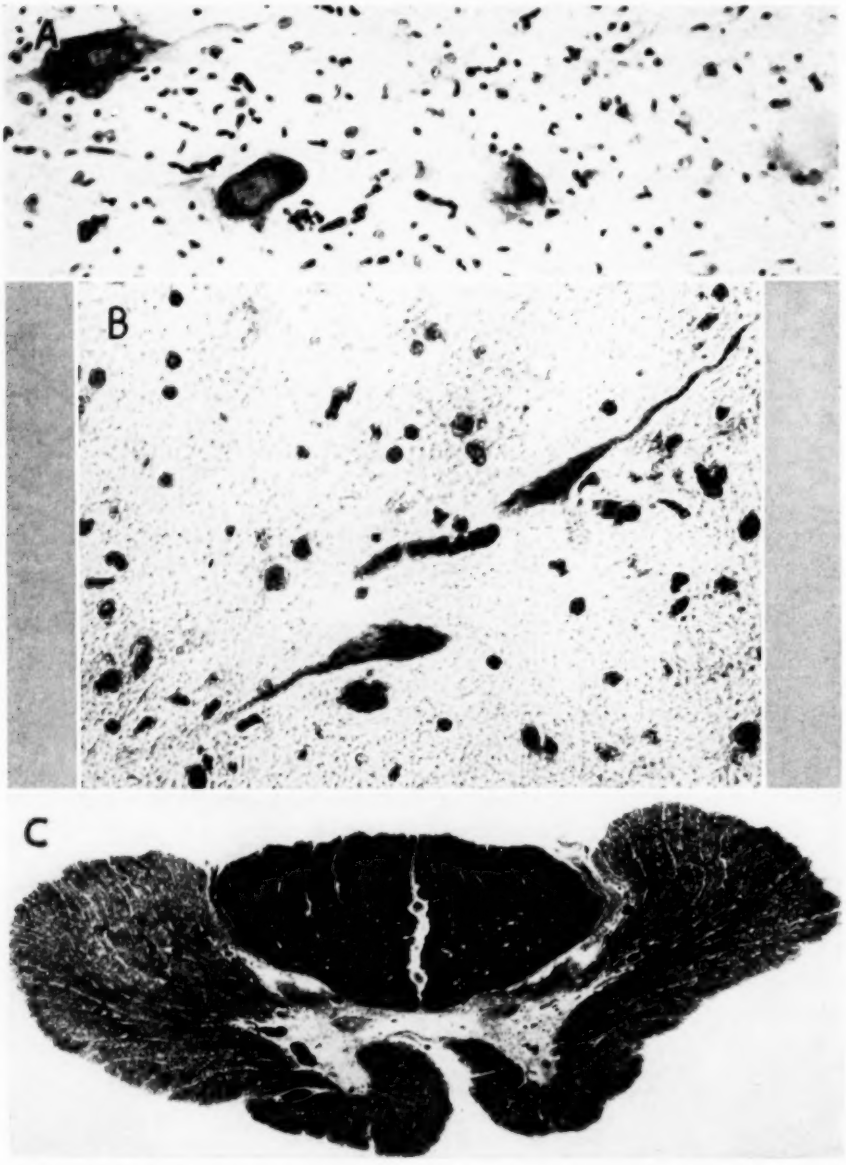

Fig. 9.—*A*, anterior horn cells in different stages of dissolution from left to right. Nissl stain; × 250.

B, pyknotic shrunken neurons in the ventral horns. Nissl technique; × 400.

C, widespread dilatation and perivascular extravasation of blood in the ventral horns and in the anterolateral funiculi. Weil stain; × 16.

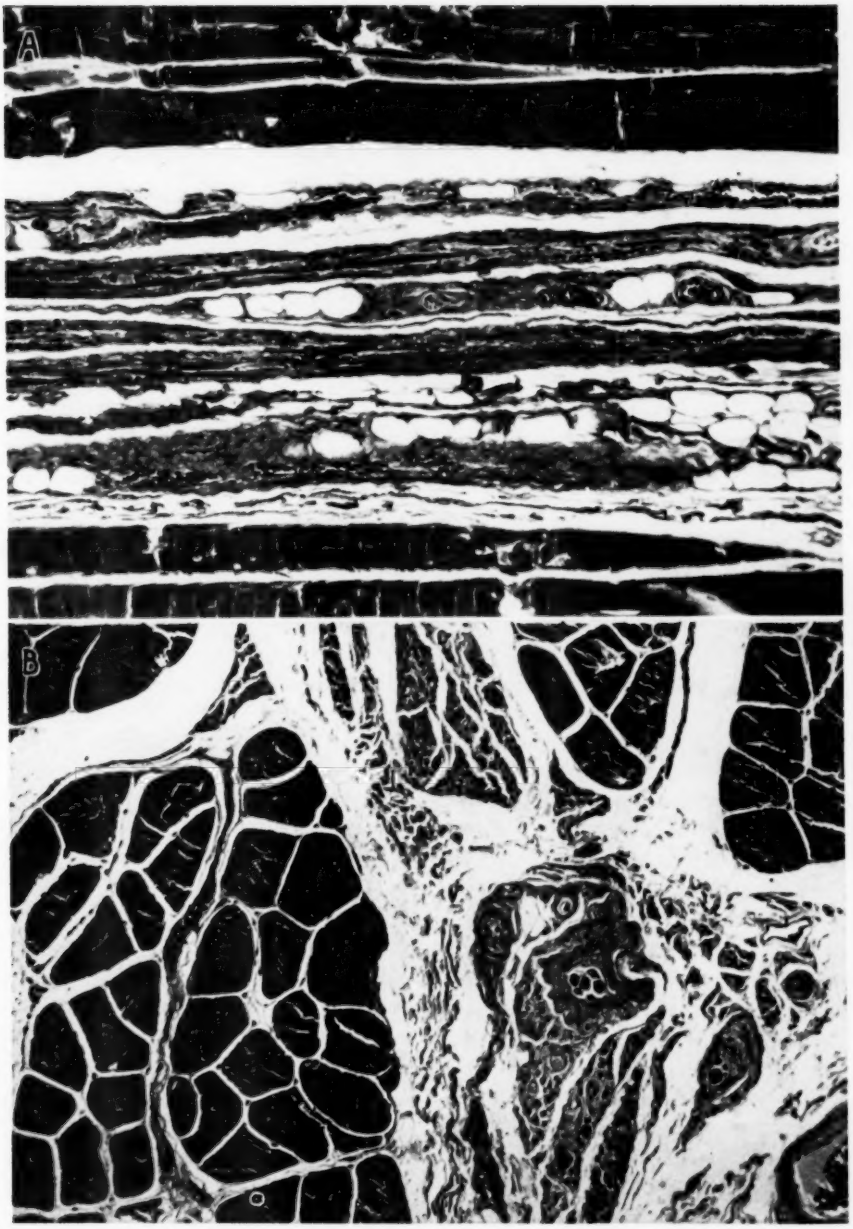

Fig. 10.—*A*, longitudinal section through the skeletal muscle. Intact fibers lie on both sides of an altered motor unit. Within the latter the fibers are shrunken; there are both proliferation of connective tissue and increase in sarcolemmal nuclei. There is also fatty tissue replacement of portions of the fibers. The alteration is present throughout the length of the fibers. Hematoxylin-eosin technique; × 120.

B, motor unit alteration shown in cross section. Compare with *A*. Hematoxylin-eosin technique; × 112.

by intercurrent diseases. Cerebrospinal fluid studies were not done in all cases, and in some instances were incomplete. In all, however, the usual determinations were within normal limits. In 36 cases in which the initial cerebrospinal fluid pressure was recorded, the average was 118 mm. of water, with extremes of 40 and 186 mm. In 40 cases the average total protein content was 40 mg. per 100 cc., with a range from 25 to 75 mg. per 100 cc. Cell counts in 29 cases ranged from none to 7 lymphocytes per cubic millimeter, the average count being 2 per cubic millimeter.

The final clinical diagnosis was accurate in all but two cases, in both of which a diagnosis of pseudobulbar paralysis was made. There were a few cases in which a clinical diagnosis of amyotrophic lateral sclerosis was made but other lesions, such as those of multiple sclerosis, were found post mortem.

Correlation of clinical and anatomic findings was satisfactory in 46 cases. In six instances clinical signs of disorder of the pyramidal tract were not found, in spite of anatomic evidence of demyelination of pyramidal tract pathways. Muscular atrophy was noted during life in all cases in this study, and disease of the ventral horn cells was seen post mortem. One patient presented generalized hyperactivity of deep reflexes but no pathologic reflexes; atrophy of skeletal musculature was general, being most pronounced in the hands. Postmortem study of the nervous system revealed much more involvement of pyramidal tract fibers than of ventral horn cells.

COMMENT

The systematized character of the anatomic alterations of the nervous system in all cases reviewed was one of the most striking facts to emerge from this study. In the two cases designated as instances of progressive spinal muscular atrophy the changes were predominantly in the lower motor neuron. The upper motor neuron changes were not associated with descending demyelination. In the other cases alterations of cells of the cerebral cortex were always found (Table 2); these were noted especially in the Betz cell area but were frequently widespread. This cerebral alteration was accompanied by demyelination of the corticospinal tracts. It is our concept that the demyelination of the pyramidal tracts so characteristic of amyotrophic lateral sclerosis is a reflection of disease of the cells of origin. This is contrary to the view that demyelination may begin anywhere in the course of the corticospinal tract.[9d] It is true that often the changes in the spinal cord are recognized more easily, but this is dependent on certain technical factors. However, there were several cases in this series in which the changes in the myelin sheaths of the corticospinal tract were most pronounced in the upper portions of the neuraxis and were less apparent in the spinal cord. The conditions discussed here are, therefore, properly designated as "motor neuron disease," since it is always the motor neuron and its axon that are altered.

It is usually easier to recognize demyelination of the corticospinal tract in the medullary pyramids and in the spinal cord because the fibers are more compact in these locations. In the internal capsule there are so many other fiber tracts that it may be difficult in routine coronal sections to find the relatively few affected sheaths or axis-cylinders of the corticospinal tract. When the Weil technique is used, the difficulties are even greater, because of the artifacts inherent in this method. We find

this stain of value mainly for topographic purposes. The lack of preliminary mordanting results in alterations of myelin and blurring of outlines, changes which do not occur in material stained by the Pal-Weigert or the Spielmeyer method. Even with the use of the latter methods difficulty may be encountered if dedifferentiation is not great enough, because of the large masses of intertwining fibers in the internal capsule. Single coronal sections of the internal capsule, unless ideally situated, cannot contain many fibers of the corticospinal tract. The Marchi technique is of limited value, since it gives positive results only in certain stages of myelin degeneration. The Sudan technique is much more valuable and should be utilized, but it, too, has limitations; old demyelination may be present even though the stain for fat is negative. We found that the presence of gliosis, as evidenced by cellular and glial stains, such as the Holzer technique, was of value in determining the presence of alterations in this difficult region and elsewhere.

The major part of the lateral corticospinal tract is situated posteriorly in the lateral funiculus of the spinal cord. The widespread demyelination of both anterior and lateral columns has been known, but receives further confirmation from this large series of cases. The most characteristic myelin-sheath picture was that of widespread anterolateral demyelination, only the posterior columns being well stained. Is one justified in assuming that this anterolateral demyelination is the result of alteration of the corticospinal tract alone, or are other motor tracts involved? The present state of uncertainty as to the origin of about 95% of the fibers of the corticospinal tract in man makes this difficult to answer.[7] There must be corticospinal projections other than those from the Betz cell area, and some of these may well be from the parietal and frontal regions. It is even possible that some fibers originate in the subcortex. Since the question cannot be decided, we have assumed for the sake of discussion that the anterolateral demyelination of the spinal cord is related to the corticospinal tract. Further anatomic data may require revision of this concept. Certainly these data fit in well with the findings of neurosurgeons that section of the lateral pyramidal tract may result only in minimal motor deficit.

Betz cells were consistently altered in 49 of our cases. The presence of normal Betz cells occasionally has been reported. These rare reports may be questioned, one objection being that different areas, such as those representing the arm and leg, may be affected in different fashions. A single normal section taken, for instance, through the arm area cannot be used to deny the existence of Betz cell alteration.

There is described sometimes a discrepancy between Betz cell alteration and the amount of descending demyelination. The latter may be greater or less than would be anticipated from examination of the condition of the Betz cells. The convincing evidence of Lassek [7a] easily explains this, for the Betz cells account for about 3% of the fibers noted in the pyramids at the level of the olivary nuclei.

Anatomically, an inflammatory type of amyotrophic lateral sclerosis has been described by some authors. There was no evidence of this in any case in our large series. It was not uncommon to find a small number of perivascular lymphocytes

7. (*a*) Lassek, A. M., and Rasmussen, G. L.: The Human Pyramidal Tract: Fiber and Numerical Analysis, ibid. **42**:872-876, 1939. (*b*) Lubin, A. J.: Relationship and Function of the Pyramidal Tract, Am. J. M. Sc. **209**:111-127, 1945.

(Fig. 4*B*), especially in cases of more rapidly advancing disease; but these cells are easily explained as a reaction to a fulminant process. There was never any real evidence of meningitis or encephalitis aside from the presence of these few lymphocytes. Even neuronophagia was but rarely encountered in this autopsy material.

The absence of anatomic alteration of the sensory fiber pathways in all but one case is a point of great importance. There was never any objective sensory change, despite the presence, at least initially, of subjective disturbances of sensation in some cases. The possibility of other diagnoses should be entertained when objective sensory alterations can be demonstrated. We believe that the finding of some posterior column demyelination in one case represents an unusual complication of this disease. It should no more be considered a part of the disease than is a carcinoma of the sigmoid colon, which also occurred in one case. Failure to observe this generalization has sometimes resulted in misdiagnosis for patients with protruded cervical intervertebral disk, spinal cord tumor, or other potentially remediable condition.

Clinically, the disease, as is well known, is characterized by a progressive, unremitting course. The diagnosis is usually easy in the later stages, when fasciculations, symmetric atrophies, pyramidal tract signs, and, ultimately, bulbar paralysis make themselves evident. It is in the earlier stages that diagnosis may be difficult, and the necessity is great for awareness of differential diagnostic possibilities. In our series the onset of the disorder was oftener in the lower extremities. This is in contrast to the generally accepted idea that the disease almost invariably starts in the upper extremities. The condition may be ushered in by subjective complaints of sensory phenomena. The disease may present itself as a monoplegia, hemiplegia, or even paraplegia, for several months, although ultimately it becomes symmetric. Oculomotor paralyses are exceedingly rare, as is nystagmus. Pyramidal tract signs sometimes may not be elicited, particularly when muscle becomes involved to such a degree that response to stimulation is impossible. The patients may suffer from mental symptoms of various types, but these are usually no more than is to be expected in the presence of a severe debilitating disease. Occasionally there may be coincidental psychoses.

The clinicoanatomic correlations in this illness usually are very good. Rarely, pyramidal tract demyelination may be observed without clinical evidence of such disorder. The finding of clinical corticospinal involvement without anatomic evidence is rare.

This necropsy series furnishes additional evidence in support of the concept that progressive muscular atrophy and amyotrophic lateral sclerosis, as well as primary lateral sclerosis, are parts of one constellation. This is illustrated by the report of Swank and Putnam,[8] who studied 151 cases clinically, in 23 of which the condition was classified as progressive muscular atrophy and in 19 as primary lateral sclerosis. These figures may be contrasted with those in the present necropsy series, in which a diagnosis of progressive muscular atrophy was made in only 2 of 53 cases and in which there were no cases of primary lateral sclerosis. Despite this anatomic evidence, the clinical files of Montefiore Hospital contain 7 cases of

8. Swank, R. L., and Putnam, T. J.: Amyotrophic Lateral Sclerosis and Related Conditions: A Clinical Analysis, Arch. Neurol. & Psychiat. **49**:151-177, 1943.

primary lateral sclerosis and 40 cases of progressive muscular atrophy. These data demonstrate that when full anatomic examination is performed, most cases fall into the group in which both upper and lower motor neuron alteration is present. These considerations are equally applicable to bulbar paralysis, as has been emphasized by Wilson.[9] In cases of this disorder Betz cell and pyramidal tract alterations, as well as disorder of the medullary nuclei, are almost always present.

It is impossible by present means to explain the rare cases in which the duration is as long as 35 years, because the anatomic findings are similar to those in the usual cases of short duration. It should be noted that the anatomic changes in an old case of poliomyelitis also may be similar to those of progressive spinal muscular atrophy, although the clinical differences are obvious.

The finding of dystrophic changes in the muscles of one patient is of interest. This, also, we believe to be a complication or a coincidence, rather than a part of the syndrome. Nevertheless, it raises the question whether in a small number of cases, primary disease of the central nervous system and of muscle may not occur together. It should be remembered in this connection that atrophy of muscles in older people can be an evidence of dystrophy,[10] despite which in at least some patients late myopathies have been diagnosed as "atypical amyotrophic lateral sclerosis."

SUMMARY AND CONCLUSIONS

This report is based on a study of 53 cases of motor neuron disease, all anatomically verified. There were 51 cases of amyotrophic lateral sclerosis and 2 cases of progressive spinal muscular atrophy. These cases conform to the well-known facts that motor neuron disease affects males predominantly and occurs in adults. The clinical onset may be with sensory complaints, although objective signs of sensory alteration are rare. The series differs from many others in that onset with symptoms in the legs was almost twice as common as in the arms. The initial complaints may be one-sided for several months, in rare cases for a few years, before the spread of signs creates the classic picture of symmetric atrophies and pareses. Some patients may survive for unusually long periods, although pathologically there are no differences between these slowly progressive cases and the cases of rapid progression.

Anatomically, in all cases in which there were suitable preparations there was alteration of ventral motor cells of the spinal cord up to the Betz cells in the cerebrum. These were the significant findings in the two cases designated as instances of progressive spinal muscular atrophy. The latter usually progresses more slowly, but in time may become full-blown amyotrophic lateral sclerosis. In the other 51 cases there was, in addition, descending demyelination from the cortex through the spinal cord. It is concluded that amyotrophic lateral sclerosis is a motor neuron disease in which the demyelination is secondary to alterations in motor nerve cells. The demyelination in the spinal cord is most commonly diffuse throughout the anterolateral columns, with greatest concentration in the regions of the crossed and

9. Wilson, S. A. K.: Neurology, Baltimore, Williams & Wilkins Company, 1940.

10. Solomon, S., and Netsky, M. G.: Muscular Dystrophy of Late Onset, to be published.

uncrossed corticospinal tracts. Limitation of the changes to these tracts in the positions depicted in most textbooks of anatomy is unusual.

A single case of associated sensory tract demyelination is interpreted as a complication, rather than a part, of the syndrome of amyotrophic lateral sclerosis. Both clinically and anatomically the latter malady is limited to motor neurons and their processes.

These data offer further confirmation of the concept that motor neuron diseases form a group which includes progressive spinal muscular atrophy, primary lateral sclerosis, amyotrophic lateral sclerosis, and progressive bulbar palsy.

Mr. Antol Herskovitz prepared the photomicrographs.

GROUP THERAPY OF PATIENTS WITH MULTIPLE SCLEROSIS

A Preliminary Report

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THIS PAPER deals with the ways in which the mixed feelings of multiple sclerosis patients toward their illness affect their functioning in interpersonal relationships as seen in group therapy.

In the beginning members ignored the group work of investigating feelings. Instead, they recited their numerous somatic complaints. With the complaints was a tendency to look for *the* cause of multiple sclerosis. Underlying these reactions was an attempt to deny hostility relating to the illness. Instead, anger was masked by a cheerful attitude to the world in general. Along with this was seen an acceptance of their dependent position. There was much anxiety about discussing their deeper feelings of being a burden on their relatives. Those who were able to accept the idea that there was secondary gain in being sick were then able to make efforts to do the group work. Some members were able to extend the gain into their home life and attempt efforts at rehabilitation and toward a better self-adjustment.

An analytically oriented therapy group was formed for the purpose of investigating the problems of these patients and giving them psychiatric help. Twenty-three of the 200 available patients on the roster of the Multiple Sclerosis Research Clinic were canvassed to attend the meetings of this group. They were told that in the group they could discuss their feelings about their mutual problems in order to help themselves and one another. The general technique of investigating feelings in order to understand them and better to accept them was outlined. The turnover before the formation of a stable group of seven was large, in part because the meetings were held in the evening on state hospital grounds. Furthermore, only patients came who lived close to the hospital, who did not have young children to care for, and who could arrange for transportation. Those who were either content with their lot or too disturbed about it dropped out. Currently, of the 23 canvassed, the group consists of 5 women and 2 men, who have attended an average of 50 sessions of 1½ hours each on a once-a-week basis.

Often there was a striking discrepancy between the degree of physical disability and the degree of psychic crippling. Thus, some patients with slight disability would become depressed, withdraw from social life, and stop working on a job or at housework. Others with pronounced impediments would continue working with a rather remarkable indifference to their real physical troubles. The reverse was

This work was done at the Multiple Sclerosis Research Clinic at Boston State Hospital; Leo Alexander, M.D., Director, and was supported by a grant from the Massachusetts Chapter of the National Multiple Sclerosis Society.

also true; that is, some patients with slight disability ignored it and worked on, while others with severe disability did very little work. In all these cases the reaction to the illness was not commensurate with the degree of physical difficulty.

In the early part of the life of the group the members spent much time in discussing somatic complaints, concerned with the bowels, bladder, walking, fine movements, eyesight, numbness, tingling, or memory difficulties.

The members used the clinic investigation of diet and medication as resistance for preoccupying themselves with physical complaints and for ignoring their feelings. Soon, members began to complain of increased physical difficulty in relation to fear and other feelings. In the second session, in which 13 people were present, 1 member, who later dropped out, said: "I have bowel trouble in crowds." When their fears were related to what others would think of them the somatic complaints decreased. They would recur as a resistance to discussion of painful issues. When the latter topics were discussed, some members of the group would leave the room to go to the toilet, while others would be on the verge of tears or otherwise indicate their anxiety by wringing their hands or their withdrawal by appearing bored and going to sleep. These patients used their physical symptoms to deny for themselves the painfulness of their feelings.

The generalized somatization of anxiety in the group led to a constant seeking of a scapegoat as *the* cause of illness. The possibilities included such factors as diet, heredity, a fall, race, religion, cigarettes, emotions, and order of birth. Repeatedly each patient would test his pet theory on the group, with the ultimate result that the others demonstrated its unreality. The members also projected their loss of self-respect for having the illness. They felt that other people looked down on them and considered them drunkards because of their staggering gait. They were not entirely satisfied with the techniques of scapegoating and projection as a means of handling their aggression. This frequently led to difficulties at home, as expressed succinctly by a former member: "I'm a street angel, but a home devil."

Underlying these reactions was a denial of hostile feelings about the illness, as well as an attempt to be "good." This response is related to the findings of Harrower [1] of exaggerated submissive compliance and excessive cordiality to the outside world. For many sessions the patients had no free discussion of feelings about having multiple sclerosis. On the occasions when the group came close to discussing this subject, members would tacitly admit, "It is a bitter pill" and express much fear of what would ultimately happen to them. Often the fear of going crazy was expressed. Even in those who were obviously depressed the attitude was "Are multiple sclerosis patients always in the dumps? Not me." This was usually enforced by a plea that no one remind them of their bitter plight. When this issue was further developed in the group, some patients stopped coming. This finding is similar to that of Grinker and associates [2] that multiple sclerosis patients have a paucity of outlets for aggression.

1. Harrower, M. R.: Results of Psychometric and Personality Tests in Multiple Sclerosis, A. Res. Nerv. & Ment. Dis., Proc. (1948) **28**:461, 1950.

2. Grinker, R. R.; Ham, G. C., and Robbins, F. P.: Some Psychodynamic Factors in Multiple Sclerosis, A. Res. Nerv. & Ment. Dis., Proc. (1948) **28**:456, 1950.

The techniques described proved inadequate for handling hostile feelings about multiple sclerosis; the patients had constantly to reinforce their own poor solutions. This was clearly explained in a preliminary interview by a prospective member. He said: "I used to be easygoing . . . happy-go-lucky . . . but with this thing I can't take criticism. . . . I blow a fuse easily. . . . I don't know if it's me or my wife or this thing." This man, though mildly disabled, was generally disgruntled and wanted to stop working. Originally the denial of hostile feelings was sufficient, but with the added stress of anxiety about the disease, projection and scapegoating would not satisfactorily handle his aggression.

The secondary gains from the illness were seen in the tacit acceptance of a dependent position which was socially rationalizable and personally acceptable.

M. C., a former window washer, had a moderate amount of difficulty in walking. Since he had been unemployed for over a year and a half, he had to accept a station wagon and its upkeep to get around, as well as other gifts from his family, with the rationalization that he would some day pay them back. To round out this illusion that he helped people, he had business cards printed bearing the following inscription:

> "I expect to pass through this world but once;
> any good therefore that I can do, or any
> kindness that I can show to any fellow creature,
> let me do it now. Let me not defer or neglect it,
> for I shall not pass this way again."

He handed out these cards during his first meeting, but never after that, even though new members had since been introduced. He constantly denied having any feeling even about the slightest anxiety-provoking incident. He demonstrated clearly the need to fall back on the secondary gain from his illness.

The illusion that dependency was necessary would vanish when the patient was able to verbalize and understand his desire for dependence.

W. K. had worked a number of years for a telegraph company repairing teletype machines. At the age of 22, when his multiple sclerosis first developed, he had already been drinking excessively. Several years later he married a rather self-sufficient, aggressive, but kind woman. By the time he came to the group he had been unemployed about a year, though he had been sick for 14 years. He eagerly ventured into the group work of investigating his feelings about his illness. When the inability to express hostile feelings was discussed, he said: "Group therapy is undoing what I've taught myself to do for 14 years." By his 35th session he told the group, to their horror, that he had welcomed his illness because of the freedom from responsibility it gave him. Shortly after this, he enrolled in a business school on his own, to learn accounting and bookkeeping. Through verbalizing and understanding his own reactions, he could try to rehabilitate himself and regain his self-respect.

Sometimes silent or minimal participation was sufficient to help a patient toward self-rehabilitation.

H. J., a divorced Negro woman, aged 46, showed that she lived up to a higher code of morals than other people, whom she considered beneath her. At first she participated little in the group except to provoke others by teasing. Gradually, however, she began to use attractive brighter colors in her clothes and to seem more cheerful, though still participating little. During the 30th meeting she attended, she was incensed at having been inconsiderately left waiting in the cold at the clinic door by a driver who brought her. For the first time she was forced by circumstances to verbalize her real feelings, and she called the inconsiderate driver "a bitch." Then she began to participate more in the group discussions. Several weeks later she went out on her own and got herself a job. Thus, constant verbalizing in the group was not necessary; to verbalize appropriate feelings at a crucial point was important.

SUMMARY

The problem of the relation between the mixed feelings of multiple sclerosis patients for their illness and their ability to function in interpersonal relationships was investigated. A two-way discrepancy between degree of physical disability and the amount of psychic crippling was noted. The methods of handling painful issues by denial, being "good," somatic complaints, scapegoating, and projection were discussed. In the sessions the secondary gains from the illness which the aforementioned attitude permitted were demonstrated. The general dissatisfaction with these ways of getting along showed itself in the difficulty some of these people had in continuing at their jobs and in their unhappy home lives. In therapy, some patients were helped through constant verbalization to rehabilitate themselves, while others were helped when they were able to verbalize their feelings at crucial moments only.

PROGRESSIVE BULBAR PARALYSIS SHOWING HEREDOFAMILIAL INCIDENCE AND INTELLECTUAL IMPAIRMENT

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HEREDOFAMILIAL incidence has only rarely been reported in cases of progressive bulbar paralysis occurring in adult life. Equally rare is the reported coincidence of marked intellectual deterioration with this disease process. Both these unusual manifestations were found in the following case, which seems, therefore, worthy of detailed description and discussion.

REPORT OF A CASE

Mrs. C. S., aged 69, was admitted to the Royal Edinburgh Hospital for Mental and Nervous Disorders, West House, on March 26, 1950. She died on April 26, 1950.

Family History.—The maternal ancestry was distinguished for good health and longevity, the mother of the patient dying at the age of 91. The paternal line was described in the locality from which they hailed as possessing "a nervous streak" (Chart). The father of the patient died at the age of 69. The stated cause of death was "progressive muscular atrophy." The commencing symptoms were difficulty in articulation and swallowing, and these were succeeded by gradual loss of power in all four limbs. Mental clarity was preserved to the end. A cousin of the father died in middle life of "paralysis of the throat." A nephew of the father died at the age of 64, of bulbar paralysis. (The causes of death were checked by reference to the parish registrar.)

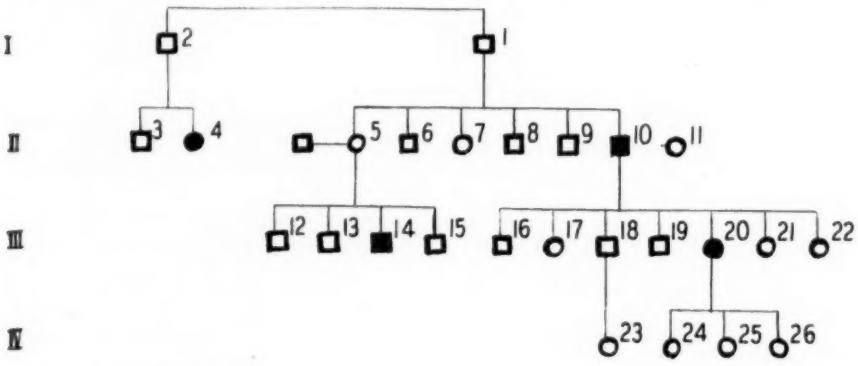
The patient was the fifth child of a family of eight. Two brothers and a sister died of childhood exanthemata. One brother died of nephritis in early adult life. Her elder, surviving brother, aged 73, is healthy; his only child, a daughter, was admitted to a hospital for mental disease at the age of 23 and died five years later, of pulmonary tuberculosis. The patient's two younger sisters, aged 65 and 60, are healthy. Both are married but childless. The patient herself had a family of three daughters, now aged 40, 39, and 31. The eldest is married. The other two daughters, both single and teachers by profession, lived with their mother.

Previous Personality.—Her history indicates that she was a woman of equable temperament and of more than average ability. A country schoolmaster's wife, she was expected to take a leading part in the social events of a small community, and until her husband's death, in middle life, of coronary thrombosis, she acquitted herself in this role with tact and skill. Friends who visited her in the hospital during her illness invariably commented on the perfection of her domestic arrangements and her gifts as a hostess.

History of Illness (Obtained from Her Two Unmarried Daughters).—Onset: 1. April-October, 1949. The first abnormal sign noted was a defect in articulation, which first showed itself in April, 1949. She began to talk more slowly, and sometimes her speech was slurred. She had no difficulty in word finding, nor did she use words incorrectly. She did not show any particular anxiety about her disability. (Since the family history must have been known to her, this in itself must be counted an abnormal sign.) She carried out her domestic and social duties with seemingly normal efficiency. In July and August, 1949, both daughters were separated from their mother for the five weeks of their annual vacation. When they returned, they noticed a considerable change in her; the articulation defect was more pronounced; there was also difficulty in swallowing, and, in the mental sphere, there was a definite falling away of interest. They

then recollected that the letters they had received from her during their holiday lacked spontaneity and had shown occasional reiterations. In one letter she referred to the nondelivery of an important domestic commodity, which they knew had arrived before their departure on holiday. In September, 1949, she first began to express delusions of a type which distressed her family exceedingly. When her eldest, unmarried daughter went out in the evening, she became agitated and expressed the conviction that she was out with strange men. (She was examined at the local hospital in September, and her illness was diagnosed as progressive bulbar paralysis.)

2. October-December, 1949. During this period the articulation defect was slowly progressive. Coincidentally, there occurred a gradual decline in intellectual capacity. She lost the ability to reason on abstract subjects, but her conversation, though more "concrete," was normal in regard to choice of words and grammatical construction. She continued to correspond with friends abroad, and the latter, reporting on these letters, said that they, similarly, showed no marked peculiarity of construction. She was still able to do her housework and cook the meals, although she occasionally asked her daughters for assistance in compiling the day's menus, assistance which she had never asked before. She still paid social visits to her



Key to genealogical tree:

1, died at age of 78; *2*, age at death unknown; *3*, died of "old age"; *4*, died of "paralysis of throat" in 60's; *5*, died of "old age"; *6*, emigrated, died "old age"; *7*, emigrated, died "old age"; *8*, accidentally drowned in early adult life; *9*, died in middle age, cause unknown; *10*, died of "progressive muscular atrophy," at age of 69; *11*, died at age of 91, siblings likewise died at advanced age; *12*, died of stroke at 65; *13*, died of enteritis at 65; *14*, died of "bulbar paralysis" at 64; *15*, emigrated and lost touch with family; *16*, died in early adult life; *17*, died in childhood; *18*, still alive, aged 73; *19*, died in childhood; *20*, the Patient; *21*, alive and well, aged 65; *22*, alive and well, aged 60; *23*, died of tuberculosis (during schizophrenic illness), at age of 28; *24*, *25*, and *26*, patient's three daughters, all alive and well.

friends, but often went at unusual times, i. e., in the middle of the forenoon. She never had any difficulty in finding her way to the homes of her friends, but on arrival there she would appear distrait in manner and doubtful as to the purpose of her visit. At certain periods, particularly at night, she would become very agitated and would then express anxious forebodings or actual delusions in relation to her daughters. Those delusions reached their peak intensity toward the end of this period, when, during the enforced absence of either of her two daughters, she would express the conviction that "they must have fallen over the rocks into the sea."

3. January-March, 1950. This period marked an accelerated decline of all abilities. She now required constant supervision; otherwise, she would wander out into the street at all hours of the day, ostensibly looking for her daughters.

Speech: Articulation became more and more difficult. At the same time there was a definite restriction in her conversation, greater than could be accounted for by the difficulty in articulation.

Writing: Her daughters, fortunately, preserved a letter she wrote to her sister in February, 1950, and this clearly illustrates the presence of aphasic defects—defects which were not obvious in speech, presumably because they were masked by the difficulty in articulation. Part of this 200-word letter is quoted:

"Dear Jessie,

"I am writing this is quite I am writing this after being at your sister Jeanie, Bob is alive few yet J.....H..... you must drive him through, all he had to do poor soap but is a lively lot. I must saw. This is at half so you can do anything. There is a suit but we are progressing poor the worst so I'll need to work round. There is plenty work so you needn't worry. You are distrest did so there is plenty. I hope you are not distared. I forgot to answer already she is such a pussy that we can get cut. If we were there I would I get I hope he is a very..... So Jeanie, must stop now, be seeing if you have got out, so "cheerio" and love from us all, Your loving sister, C.... M...." [maiden name].

This letter, with its pronounced aphasic defects, is largely unintelligible to the ordinary reader, but her daughters, aware of her thoughts and circumstances at the time of writing, were able to infer the greater part of what she was attempting to express. The striking features of this letter are its retention of conventional form, its relatively accurate beginning and ending, its normal punctuation—"cheerio," for instance, is written within inverted commas—and the legibility of the individual words.

Reading: She still read the daily papers and could demonstrate paragraphs of local interest. She tended, however, to point out the same paragraph again and again, apparently oblivious of the fact that she had previously drawn attention to it.

Orientation for Time, Place and Person: She was often confused about the time of day and would attempt to prepare luncheon dishes for the evening meal or vice versa. Disorientation for place did not occur until the end of this period, when she began to have occasional difficulty in finding her way about her own home. She never failed to recognize her friends and was always delighted to see them; but after the first exchange of greetings her attention wandered, and she took no further interest in them.

Practical Tasks: Housework. She was no longer able to organize and carry out the day's work. She no longer attempted any complicated task, such as baking; she still, however, endeavored to assist with many of the more routine and mechanical household tasks and carried these out in her former methodical manner.

Knitting. She had previously been expert at this craft, but now made numerous mistakes when attempting complicated patterns. She was able to do ordinary, plain knitting until a few weeks before admission to hospital.

Social Behavior: She no longer manipulated knife and fork correctly and would often grab articles of food from the plate. She was still able to dress herself. She was never incontinent.

Bizarre Conduct: At times she would suddenly announce that she and her daughters must set out on a visit to her sister and start packing a case for the journey. Having assembled the conventional contents of this case, i. e., nightdress, toilet articles, etc., she would then add an odd and inappropriate collection of articles, taking perhaps an ornament from the mantelpiece or a pepper pot from the table.

Emotional Abnormalities: She remained for the greater part of the time in normal emotional rapport with her daughters. She was never irritable. Flashes of her old sense of humor appeared, albeit infrequently. One such concerned one of her proposed visits to her sister. Her daughters had allowed her to make her usual preparations without argument or remonstrance. Having completed her preparations, she sat down expectantly, apparently waiting for them to accompany her. When half an hour had passed and they showed no intention of doing so, she looked over at them, smiled humorously, and said, "Well, I suppose I can just take my boots off." Episodically, she exhibited great agitation, wandering restlessly about the house, moaning bitterly, and refusing reassurance. She continued abnormally apprehensive about her daughters when they left her side, although with failing capacity, overt delusions were no longer expressed.

Clinical Examination.—The patient was a tall, erect, pleasant-looking woman, who appeared considerably younger than her actual age. Despite the physical and intellectual deterioration wrought by her illness, she still radiated an indefinable air of distinction, which enabled the onlooker to appreciate the strength of her previous character and personality.

General Behavior: This alternated from hour to hour. For short periods she lay quietly in bed; then she became restless, constantly pushing the clothes aside and making endeavors to get out of bed. When allowed up, she walked quickly and apparently purposefully around the ward. Often she shook hands with all the other patients and appeared hurt and somewhat nonplussed if they did not respond in conventional fashion to her greetings. She avoided all obstacles to her progress with ease. After getting her bearings, which took her a few days, she was able to return from the examination room, at the end of the corridor, to her own bed, in the corner of the observation ward. Periodically, on an average once a day, she became abnormally distressed, sitting up in bed, rocking from side to side, moaning piteously. No verbal reassurance would quiet her on these occasions. She was always delighted to see her daughters, greeted them affectionately, and was always quiet and placid while they were with her.

She seemed unconcerned about the staining of her clothes by the constant dribbling of saliva. If a cotton apron was draped about her day dress for its protection, she removed it indignantly, apparently considering its presence unseemly. She would leave the apron in situ, however, if she was given a duster and allowed to dust the ward, which she did with great thoroughness, although frequently showing an inappropriate choice of objects whereon to carry out this activity. She was able to take her own food, but did this in a clumsy, untidy manner, setting down her cup on the counterpane or the edge of the table, not comprehending that it will fall over in these precarious positions.

Examination of Intellectual Faculties: (This examination was rendered laborious by reason of her poor powers of concentration and early fatigue. She tried hard to cooperate and was pleased when encouraged. Her pleasure at success was, however, restrained; her reaction to her success was one of boredom; she lost interest and looked around for something fresh to take up her attention.)

1. Speech. She had obviously great difficulty in articulation. She did not always try to enunciate words, either in response to objects shown or to simple inquiries of a personal nature. Incidental speech was better than deliberate; she frequently uttered a surprisingly intelligent and reasonably articulate phrase to a member of the nursing staff, indicating that she had some knowledge of her present whereabouts. During formal examination, however, such utterance was rare, and was confined to infrequent monosyllabic recognition of objects.

2. Eliciting of information by writing. (*a*) Naming of objects. Given a pad and pencil, she wrote down, firmly and unhesitatingly, the names of common objects shown to her, i. e., ring, keys, and pin. Asked to write down the material of which they were made, she also answered correctly, e. g., "ring—gold."

She responded similarly when shown pictured objects, e. g., eggs in red egg cup, "egg cup full"; red and green apples, "apples." She was not always able to give the color of the objects presented to her.

(*b*) Response to questions of personal interest. She was able to write her own name, and when asked the names of each of her three daughters, she responded by writing down the full Christian name, middle name, and surname of all three. She gave her own date of birth correctly as 1881, but gave erroneous dates for the birth years of her three daughters, on one occasion perseverating by writing 1881.

3. Response to commands. She obeyed correctly simple commands relating to her own body and showed no defect of laterality.

4. Approximation of written and spoken names to pictured objects. A row of pictures of simple objects were placed before her, and she was handed name cards and asked to place them on the appropriate pictures.

This she did correctly on two occasions, but then her attention wandered and she had to be coerced to place the third card. She finally achieved this correctly but resolutely refused to attempt a fourth. (Throughout all such tests, the stimulus had to be changed frequently to gain a response.)

5. Copying of designs. She copied successfully a design of three matches. A design of five matches was copied with partial success—she succeeded in placing three of the matches correctly, and it was noteworthy that she was able to do this in a different plane from that of

the specimen design. She copied correctly the diagrammatic drawing of a face. She could copy simple geometrical figures, like squares and a triangle, and did this in a normal manner, and not in the manner of some patients with organic defect, who draw the figure in one continuous line.

Physical Examination.—The patient was a woman of spare build but good nutrition. No abnormality was found in any system other than the central nervous system. The blood pressure was 150/100. The Wassermann reaction of the blood was negative.

The optic fundi were normal. The right pupil was larger than the left, but the pupillary reactions were preserved. Sensibility over the face was unimpaired. The jaw jerk was not increased. There was a definite fixity of expression. (On her greeting someone known to her, the patient's eyes lighted up, but only a trace of a smile appeared, and that in the upper part of the face.) There was marked atrophy of the orbicularis oris, with eversion of the lips, but other facial muscles appeared unaffected. Hearing was apparently intact. Position and movements of the soft palate were normal. The pharyngeal reflex was very brisk, as shown by the response to laryngoscopic examination. The vocal cords moved normally; phonation and coughing were retained. There was no paralysis or wasting of the sternocleidomastoid and trapezius. The tongue showed bilateral wasting with constant vermicular fibrillation and could be projected only tremulously to the lip margins. There was slight atrophy of the thenar and hypothenar eminences of both hands, but the motor power was relatively well preserved. No atrophy of the muscles of the arms and shoulder girdle, and no fibrillary tremors were noted. The lower limbs showed no abnormality. All proprioceptive and cutaneous reflexes were normal. Sensation was unaffected. Sphincter control was intact.

A roentgenogram of the skull showed a slight degree of internal hyperostosis in the frontal area.

Cerebrospinal Fluid: Manometric tests showed no abnormal rise of pressure. The protein content was 30 mg. per 100 cc.; the cells, 3 per cubic millimeter; the Wassermann reaction was negative; the colloidal gold curve was 0000000000.

Later Course of Illness.—The condition of the patient remained relatively unchanged for three weeks. On April 20, 1950, mild pyrexia developed. The following day she was quite unable to reply to any question in writing and responded merely by meaningless scribbles. She recognized her friends when they called to see her. Her condition deteriorated, and she died on April 26.

Autopsy.[1] The autopsy was carried out within two hours of death.

Lungs: There was moderate hypostatic congestion of the posterior borders and of the bases.

Heart: The coronary arteries showed fairly severe atheroma with patchy calcification. The heart was small and showed moderate brown atrophy.

Stomach and Duodenum: In the distal part of the jejunum were two small intramural nodules of firm tissue. On microscopic examination they showed the structure of typical carcinoids (argentaffin carcinoma) and were seen to be invading the muscular and serous coats.

Brain: After fixation. The leptomeninges showed slight opacity over the two frontal lobes. The vessels at the base showed only minimal atheroma. There was gyral atrophy throughout all lobes of both cerebral hemispheres, being most marked in the two frontal lobes.

Microscopical examination. Frontal lobes. There was moderate loss of nerve cells, and many of those surviving showed brown lipochrome pigmentation. Argyrophile plaques were scattered throughout the cortex, but not in such numbers as to suggest senile dementia or Alzheimer's disease. Astrocytic proliferation (Cajal's stain) was seen in relation to many plaques, but diffuse gliosis was not present. Neurofibrillary tangles within nerve cells were not seen. The white matter was normal. There was no evidence of vascular or inflammatory disease.

Temporal lobes. There was only moderate loss of nerve cells in the cortex, with the presence of an occasional senile plaque.

Motor cortex. Loss of and atrophy of large pyramidal cells were present, with pigmentation of many other nerve cells. No other changes were present.

Occipital lobe. No abnormalities were noted except for pigmentation of some nerve cells.

1. The autopsy was carried out by Dr. W. Forbes, Department of Neuropathology, Edinburgh University.

Hippocampus. There was moderate loss of nerve cells from the vulnerable (Sommer's) sector of the pyramidal cell layer.

Basal ganglia; midbrain; pons. No abnormality was noted.

Medulla oblongata. There was bilateral atrophy of nerve cells in the hypoglossal nucleus, with distortion and pigmentation of many surviving cells. Astrocytic proliferation accompanied this nerve cell loss. The dorsal motor nucleus of the vagus showed slight atrophy on both sides.

Spinal cord. No evidence of demyelination of any column was found. There was moderate atrophy of the motor nerve cells in the anterior horns in the cervical and upper dorsal regions, with pigmentation of surviving cells and astrocytic proliferation.

Clinicopathological Correlation.—1. Physical Findings: Clinically, this patient showed the signs and symptoms of classic progressive bulbar paralysis of the atrophic type. The tongue showed constant vermicular contractions and could not be protruded beyond the lips. The orbicularis oris was wasted; the lips were everted, and saliva dribbled continuously from the mouth. Articulation of speech was grossly affected; phonation remained, but the pitch of the voice could not be altered, so that all utterance degenerated into a monotonous, largely unintelligible wail. Swallowing was difficult and attended with frequent regurgitation. The upper facial muscles were characteristically little affected. Likewise, the typical immunity of the pharyngeal constrictors in this disease (Martin[2]) was well illustrated when laryngoscopic examination was attempted, since this resulted in immediate spasm of the pharynx.

Clinical evidence of minimal spinal involvement was present in the form of slight, but obvious, atrophy of the thenar and hypothenar muscles of both hands.

The histopathological picture was in agreement with the clinical findings. The motor cortex showed diminution and atrophy of large pyramidal cells, with pigmentation in many of those remaining, such as is commonly found in motor neurone disease whatever the varying involvement of structures below this level. The only cranial nerve nucleus showing gross bilateral pathological change was the hypoglossal. The nucleus of the facial nerve was reported as normal, and, in view of the atrophy of the orbicularis oris seen clinically, this tends to confirm the suggestion "that the orbicularis oris may be innervated by part of the hypoglossal nucleus, fibers from which join the facial nerve" (Brain[3]). The moderate atrophy of anterior horn cells in the cervical and upper dorsal regions was in harmony with the clinical finding of slight bilateral atrophy of thenar and hypothenar muscles. There was no evidence of demyelination of the columns of the spinal cord. Clinically, also, a spastic element was noticeably lacking. The combined pathological and clinical findings therefore stress the predominance of a nuclear amyotrophy in this case of motor neurone disease.

2. Intellectual Impairment: Coinciding with the onset of the physical illness and showing a similar, inexorable progression were intellectual defects of a type characteristically found in cortical atrophy or destruction. The relationship between mental symptoms and the cortical lesions found at autopsy will be considered in the next section.

COMMENT

Heredofamilial Incidence in Motor Neurone Disease.—The term motor neurone disease is here used advisedly to comprehend progressive bulbar paralysis, amyotrophic lateral sclerosis, and progressive muscular atrophy. It is accepted that all three denote a common disease process which attacks both upper and lower motor neurones, the varying nomenclature depending on the site of the greatest predilection. It is also accepted that none of the designations is mutually exclusive.

1. Familial Incidence: Numerous instances have been reported of the occurrence of the disease in two or more siblings. The majority of cases of sibling incidence concern children or adolescents; and when due allowance has been made for the

2. Martin, J. P.: Price's Textbook of Medicine, Ed. 7, London, Oxford University Press, 1947, p. 1771.

3. Brain, W. R.: Diseases of the Nervous System, London, Oxford University Press, 1947, p. 1771.

characteristic variability found in this disease, it is still true to state that these childhood cases often differ markedly from comparable adult forms of the illness. To mention one important difference, the duration of the illness is very much longer. Kinnier Wilson,[4] after enumerating these familial cases, adds the significant footnote, "Some of these familial amyotrophic or bulbar cases show features so alien to the generic picture as perhaps to be wrongly included in the class." In this connection, however, it is fair to point out that the original authors do not always claim the clinical title attributed to them by later commentators. A case of Gordon Holmes [5] which concerns two sisters, aged 15 and 13, is often cited as an instance of familial amyotrophic lateral sclerosis. Yet the author designates this personal case, and six similar cases collected from the literature, as instances of "family spastic paralysis associated with amyotrophy," and is careful to point out that these childhood cases appear to constitute a definite entity of their own.

From these examples, and there may be many more in the literature, it seems justifiable to group such cases into a definite class, of which the family affection, the onset in early life, and the tendency to slow progression of the symptoms, are the distinguishing features.[5]

2. Direct Inheritance: In contrast to the relatively numerous, but rather atypical, cases of familial incidence in youthful patients, reported cases of direct inheritance are extremely rare, but in the latter the disease process is more typical and the patients belong to an older age group. Bernhardt [6] (1889) described the cases of two cousins, the children of two sisters. Both mothers were stated to have died of progressive muscular atrophy of the Aran-Duchenne type. One cousin, when first seen, at the age of 30, suffered from atrophy of the neck and shoulder muscles. He later had bulbar symptoms and died within three years of the appearance of the first symptoms. The other cousin, first seen at the age of 40, had typical amyotrophic lateral sclerosis with bulbar palsy, weakness and fibrillary tremor of the right arm, and spasticity of the legs and died within two years. Gowers [7] (1892), in his textbook, mentioned the above cases, and also referred, unfortunately without giving details, to a case of his own. The relevant paragraph is perhaps worth quoting, since he reechoes Kinnier Wilson's warning on the atypical form of so many cases of sibling incidence, as opposed to the clearer-cut syndrome found in reported cases of direct inheritance.

Rarely there is direct inheritance of the disease. Among instances I have met with are a lady whose mother died from a similar atrophy, and another case in which a brother died from some chronic disease of the cord, attended with wasting, but three cases of bulbar symptoms have been recorded, two of whom were cousins, the children of two sisters, the third who had had syphilis was a cousin, but his affection was untypical. Direct inheritance seems to be most common in cases that occur late in life. When many members of a family suffer from muscular atrophy, the malady is nearly always myopathic and not spinal.

More recently, Lovell [8] (1932) has reported a case of progressive bulbar palsy in which inheritance followed the same pattern as that shown in Bernhardt's cases. The patient, a woman of 66, was seen in May, 1931, when she complained of

4. Wilson, S. A. K.: Neurology, London, Edward Arnold & Co., 1940, p. 1008.

5. Holmes, G.: Rev. Neurol. & Psychiat. **3**:256, 1905.

6. Bernhardt: Virchows Arch. path. Anat. **115**:197, 1889.

7. Gowers, W. R.: Diseases of the Nervous System, Ed. 3, London, J. A. Churchill, Ltd., 1897, p. 533.

8. Lovell, H. W.: Arch. Neurol. & Psychiat. **28**:394, 1932.

drooling of saliva and difficulty in speech, the latter of eight months' duration. Neurological examination revealed weakness of the perioral muscles, atrophy and fibrillation of the tongue (which could not be extended beyond the gingival margin), dysarthric speech, laborious deglutition, slight weakness of the pharyngeal muscles, but no paralysis of the larynx. The knee jerks were increased, but other deep reflexes were normal and the plantar response was flexor. The patient was followed up for three months, at the end of which time physical symptoms were more marked but intellect appeared unimpaired—"She expressed her thoughts in writing, which she did well." Investigations of this woman's family history showed that her mother had died of progressive bulbar palsy at the age of 65, after a year's illness. Her mother's brother died at the same age of the same disease, and his son, the patient's cousin, died at the age of 55, again of the same disease. No other relatives in the two generations were affected. Lovell's conclusion was that the "disease appears to be transmitted by a recessive, non-sex-linked mendelian trait." Gates,[9] however, in his book entitled "Human Genetics," examines this case described by Lovell and considers that the genetic basis is more likely to be an irregular dominant.

In our case, the hereditary pattern is similar to, but not identical with, that seen in the cases described by Bernhardt and Lovell. In their cases two affected siblings each had one child who suffered from a similar disease. In our case two first cousins were affected in each of two successive generations. The patient was the child of an affected father—the father's first cousin and the father's nephew both died of a similar disease. No consanguineous marriages could be traced. The patient's maternal ancestors had been distinguished for their good health and remarkable longevity. It is difficult, therefore, to reconcile this type of inheritance with a recessive gene. It is easier, and not less likely, to postulate the operation of an autosomal dominant gene, showing a certain irregularity in its expression. It has to be remembered that the disease process under consideration did not show itself until the affected members were well into their seventh decade.

> The main difficulty in dealing with conditions of very late onset is that many of the members of the pedigrees who actually have the gene or genes making for the condition will not display it because either they will die before the age when the condition will become manifest, or possibly they may have symptoms, but they will be lost sight of as they may also be suffering from some other serious unrelated condition.[10]

Mental Symptoms.—There is no lack of cases in the American and Continental literature testifying to the occasional occurrence of mental symptoms in motor neurone disease. Study of the available material reveals, however, two important defects: (*a*) Many of the cases described lack histopathological verification, and (*b*) the authors do not always attempt to distinguish between symptoms characteristic of the "functional psychosis" and those met with in true organic deterioration. The latter omission has been commented on by Wechsler and Davison,[11] in a brief survey of the literature, attached to their clinical and pathological description of amyotrophic lateral sclerosis with mental symptoms. They remarked that "in order to say with assurance that the pathological process causing amyotrophic lateral sclerosis is also capable of bringing about mental symptoms, the clinical picture

9. Gates, R. R.: Human Genetics, Ed. 3, New York, The Macmillan Company, 1946, Vol. 2, p. 1054.

10. Crew, F. A. E.: Personal communication to the author.

11. Wechsler, I. S., and Davison, C.: Arch. Neurol. & Psychiat. **27**:859, 1932.

would have to resemble an organic dementia and not a manic-depressive or other so-called emotional or psychogenic psychosis." For the sake of brevity and simplicity, only authors who have admitted this distinction, and have referred to autopsy findings, will be cited here. Van Bogaert [12] (1925), in a series of 31 cases of amyotrophic lateral sclerosis, personally observed, found mental symptoms virtually absent in 19, a recognizable emotional accentuation present in 2, and what he regarded as a specific mental state comprising both emotional and intellectual defects present in the remaining 10. These 10 cases are carefully described—in one at least the defect was verified pathologically—and the description of the emotional and intellectual changes found clearly demonstrates their organic basis. The only criticism which can be made of this large series—the largest in the literature—is that the author is so preoccupied with establishing a specific affective state as characteristic of amyotrophic lateral sclerosis that he has dismissed somewhat summarily the equally important accompanying aggregation of intellectual defects. All 10 patients showed defects in memory, attention, and judgment; some were disorientated, and one showed a jargon aphasia. In many, the intellectual defects progressed to an end-state of profound dementia. In 9 of the 10 cases were bulbar symptoms present—in only one case was the disease process confined to the spinal cord.

Wechsler and Davison [11] (1932) described three cases with autopsy findings. The first case concerned a man of 38 "with nuclear involvement mainly of the bulb and upper part of the spinal cord, and pyramidal tract disease." In the other two cases muscular atrophies and pyramidal tract signs were combined with extrapyramidal disease. All three patients showed progressive intellectual impairment. In a later article, one of the co-authors, Davison [13] (1932), published the latter two cases as examples of spastic pseudosclerosis, or Jakob-Creutzfeld disease. Only the first case, therefore, will be considered here. Mentally, the patient was described as "congenial but not capable of co-operating." He knew his own name, was "slightly interested in his environment as long as there were variations," could obey simple commands, but could not carry out complicated acts. His speech defect consisted of both aphasia and dysarthria. Death occurred within three years of the appearance of the first symptoms, spinal symptoms having preceded bulbar. In addition to pathological changes in the brain and spinal cord characteristic of amyotrophic lateral sclerosis, widespread diffuse cortical changes were noted. The frontal convolutions showed marked atrophy. Histopathological examination of the area extending from the frontal to the temporal region revealed distortion of cortical architecture, diminution of ganglion cells, nonspecific changes in many of the ganglion cells remaining, the process being more pronounced in the fifth and sixth layers, and moderate glial proliferation. Since these changes existed in addition to the alterations in the Betz cells characteristic of amyotrophic lateral sclerosis, the authors considered that "in this case the disease had lost its selective character" and concluded that "the degenerative process underlying the motor syndrome was also responsible for the organic psychosis."

Meyer [14] reported the case of a man aged 55 with a combination of spinal and bulbar signs characteristic of amyotrophic lateral sclerosis and, in addition, mental

12. van Bogaert, L.: Encéphale **20**:27, 1925.

13. Davison, C.: Brain **55**:247, 1932.

14. Meyer, A.: Ztschr. ges. Neurol. u. Psychiat. **121**:107, 1929.

symptoms which commenced as personality changes and progressed to complete dementia. The duration of the illness was nine months. The very detailed pathological findings accompanying this case can be summarized only briefly. In addition to the lesions in the brain and spinal cord characteristic of amyotrophic lateral sclerosis, a widespread, subacute degenerative process involved the cortex, particularly the temporal and precentral regions, the globus pallidus, the medioventral thalamic nuclei, the subthalamus, and the tuber cinereum. This process was characterized by reduction and degeneration of ganglion cells with marked glial proliferation. A mild mesodermal reaction was evident, with hyperplasia of vessels and some perivascular infiltration. In the cortex, nerve fibers, as well as ganglion cells, were implicated, with corresponding glial overgrowth. Meyer compared the clinical and pathological findings in this case with those found in Jakob-Creutzfeld disease and concluded that his case "forms a bridge" between the latter disease and amyotrophic lateral sclerosis.

Worthy of emphasis is the finding that all but one of the above cases of motor neurone disease with mental symptoms showed the medullary nuclei involved. The significance of this is not known. Certainly, mental symptoms are common in cases of bulbar lesions, particularly when the supranuclear neurones are involved, as in "pseudobulbar paralysis" and in the spastic type of progressive bulbar paralysis. In the latter, however, the mental syndrome usually described is that of "spasmodic laughing and crying," and this formed no part of the symptoms in the cases under review.

It is interesting, also, to speculate whether intellectual deterioration may sometimes go unnoticed in patients with progressive bulbar paralysis because of (*a*) their articulation defect, (*b*) the distressing and disabling nature of the infirmity, and (*c*) the relatively short period of observation, since the onset of bulbar symptoms implies rapid progression to a fatal end. While this supposition might be accepted in regard to mild intellectual defect, it is difficult to believe that the more massive and flamboyant "organic psychoses" described in relation to the present series of cases could go unnoticed if they occurred with any degree of frequency. It must be assumed, therefore, that this severe type of intellectual deterioration is a rare manifestation of motor neurone disease. The question then arises whether the mental symptoms of organic deterioration are an expression of the same disease process as that causing the physical symptoms. The authors of the cases so far described have replied in the affirmative. Van Bogaert goes so far as to draw an analogy between his cases of amyotrophic lateral sclerosis with mental symptoms and Huntington's chorea, pointing out that in the latter disease the motor disorder is based on a lesion of the corpus striatum, while the mental symptoms arise from an extension of the same disease process to the cortex. Certainly, if this explanation is not accepted, it is difficult to prove an accompanying second disease process as the cause of the mental symptoms in the cases described by Wechsler and Davison, van Bogaert, and Meyer and in the case which is the subject of the present paper. The pathology of my case—marked gyral atrophy, diminution of ganglion cells, and glial proliferation in the cortex of the temporal and frontal lobes—is similar to that in the case described by Wechsler and Davison. An additional finding in the present case is the presence of occasional argyrophile plaques, and these, considered in conjunction with the age of the patient, could be used as an argument to

prove that the mental symptoms were merely the result of senile change. Senile plaques, however, are frequently found in the brains of aging patients who have shown no intellectual defects in life. The pathological report in the present case stresses that, although senile plaques were present in the cortex of the frontal and temporal lobes, they were not so numerous "as to suggest senile dementia or Alzheimer's disease." An even more cogent argument against such a hypothesis in this case is the clinical course of the intellectual deterioration, which in no way resembled that found in senile dementia. The history and results of mental examination in the case have been described in some detail in order to bring out this difference. The sudden onset, the rapid progression, the unequal dropping out of specific faculties, and the aphasic defects, illustrated in a letter written by the patient two months before her death, all make it difficult to explain the mental symptoms in terms of mere involutionary change. It therefore seems reasonable to conclude that the intellectual deterioration described is based on a cortical extension of the same disease process as that causing the physical symptoms.

In conclusion, a brief reference should perhaps be made to the close affinity existing between such cases of amyotrophic lateral sclerosis with mental symptoms and the disease described by Creutzfeldt [15] (1920) and Jakob [16] (1921). As described by Jakob, this syndrome consists essentially of the triad (1) mental changes based on cortical lesions; (2) extrapyramidal disease, and (3) involvement of bulbar motor nuclei, anterior horn cells, and descending corticospinal tracts, similar to that found in motor neurone disease. The etiology of the condition is unknown. In the cases considered in the foregoing pages, symptoms of extrapyramidal disease were not present. It therefore seems wiser at this juncture to group them in a separate category. The similarities and differences existing between the two groups have been tabulated by Meyer.[14] Heredofamilial incidence has occasionally been reported in Jakob-Creutzfeld disease. It may well be, therefore, that we are dealing with a similar disease process which in some cases diffusely affects the cortex, bulbar motor nuclei, anterior horn cells, and descending corticospinal pathways and in others extends to involve the extrapyramidal system.

SUMMARY

A case of progressive bulbar paralysis is described the symptomatology of which conforms to classic descriptions of this disease entity.

Unusual concomitants in this case were (*a*) the heredofamilial incidence, and (*b*) mental symptoms of the type found in organic intellectual deterioration.

While each of these unusual features has been reported separately in cases of motor neurone disease, their association in one particular case has not so far been reported.

It is concluded that (*a*) the genetic basis is an autosomal dominant gene showing irregularity in its expression, and (*b*) the accompanying mental symptoms are caused by cortical extension of the disease process, producing the physical symptoms.

15. Creutzfeldt, H. G.: Ztschr. ges. Neurol. u. Psychiat. **57**:1, 1920.
16. Jakob, A.: Ztschr. ges. Neurol. u. Psychiat. **64**:147, 1921.

HEMANGIOMAS OF THE PONS

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TUMORS of the pons are not common. McLean [1] stated: "The slowly growing, relatively infrequent tumors of this region produce a kaleidoscopic wealth of signs which are myriad combinations of nuclear paralyses and projection-tract disturbances, a neurologic delight for diagnosis and neurosurgical despair for therapeusis."

The vascular tumors constitute only a very small portion of these tumors and are thus extremely rare.

A certain confusion still prevails with regard to the nomenclature of the vascular tumors of the central nervous system. Virchow [2] classified the angiomatous anomalies as follows:

1. Cavernous angiomas, i. e., vascular tumors made up of dilated "cavernous" spaces with fused walls, so that neither glia nor specific nerve tissue, but only a sparse stroma resembling connective tissue, is found between the spaces
2. Vascular changes in which glia or nerve tissue is present between the individual lumina
   (*a*) Telangiectases (or simple angiomas), consisting of vessels of capillary structure
   (*b*) Racemose angiomas, consisting of vessels resembling both arteries and veins

Cushing and Bailey [3] classified only the second group as malformations, while they regarded the cavernous angioma as a true neoplasm.

Bergstrand and associates,[4] who in all essentials followed Virchow, called Virchow's second group racemose angiomas and subdivided it as follows: (*a*) telangiectases, (*b*) Sturge-Weber disease, (*c*) arterial racemose angiomas, (*d*) venous racemose angiomas, and (*e*) arteriovenous aneurysms.

Bergstrand was aware of the existence of transitional forms between cavernous angiomas and telangiectases, and Sjövall and Lundgren [5] took the view that if a

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1. McLean, A. J., in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Julius Springer, 1936, Vol. 14, p. 201.

2. Virchow, R.: (*a*) Die krankhaften Geschwülste, Berlin, A. Hirschwald, 1863, Vol. 3, p. 306; (*b*) Über die Erweiterung kleinerer Gefässe, Arch. path. Anat. **3**:427, 1851.

3. Cushing, H., and Bailey, P.: Tumors Arising from the Blood Vessels of the Brain, Springfield, Charles C Thomas, Publisher, 1928.

4. Bergstrand, H.; Olivecrona, H., and Tönnis, W.: Gefässmissbildungen und Gefässgeschwülste des Gehirns, Leipzig, Georg Thieme, 1936.

5. Sjövall, E., and Lundgren, N.: Zur Kenntnis des Angioma simplex cerebri (Telangiectasien), Acta path. et microbiol. scandinav. Supp. 37, p. 476, 1938.

change should be made in Virchow's original classification, cavernous angiomas and telangiectases should be grouped together, as distinct from Sturge-Weber disease and vascular tumors made up of arterial and venous vessels.

As a further justification for this rearrangement, it was stated that in the first two forms of tumor there are no changes in the pial vessels, while such changes are constantly present in Sturge-Weber disease and are conspicuous in racemose angiomas (in Virchow's sense). However, transitional forms between telangiectases and racemose angiomas may also be encountered; the presence of capillaries, veins, and arteries has been reported several times (Brock and Dyke's Case 8 [6]; Leyser [7]); accordingly, there are no grounds for maintaining a sharp distinction between these two forms. At variance with Bergstrand's classification, Manuelidis [8] expressed the view that there is no reason for maintaining the group of arterial racemose angiomas, since no case of such a type has been convincingly demonstrated. This was admitted by Bergstrand, who, like Cushing and Bailey, found that this term had to denote angiomas supplied from and draining into arterial vessels. Manuelidis, on the other hand, pointed out that this classification is not purely a histologic one. He reported that in Sturge-Weber disease all the various histologic pictures may be encountered. According to Manuelidis, the classification should be as follows: (*a*) telangiectases, (*b*) cavernous hemangiomas, (*c*) venous hemangiomas, and (*d*) arteriovenous hemangiomas. It should be added that transitional forms may be found.

REPORT OF PERSONAL CASES

Case 1.—A man, born in 1910, had been in perfect health up to the time that the initial symptoms of his present disease appeared, at the end of 1946. The symptoms were difficulty in looking to the side with the left eye, diplopia, slight unsteadiness of gait, and a tingling sensation in the tips of all the fingers. These symptoms lasted about one month.

In March, 1947, similar symptoms developed, this time accompanied by tingling sensations in the right arm and the right side of the head and by dysesthesia of the entire right half of the body. The symptoms subsided in the course of about three months. He was hospitalized in the State Department of Neurology at the City Hospital, Aarhus, from June 12 to July 7, 1947, with the diagnosis of pontine encephalitis. A pronounced nystagmus on looking to the right, paralysis of movements of the left eye to the left, and difficulty in moving the right eye to the left were noted. Ophthalmoscopic examination did not reveal any abnormalities. The audiogram was normal; there was a coarse downward nystagmus with the patient in the dorsal recumbent position, and the caloric test with injection of hot water into the left ear produced a brief, normally directed nystagmus, followed by conjugate deviation to the right. The postrotatory and caloric reactions were both very weak, of short duration, and accompanied with very slight movements. The abnormalities observed were suggestive of a central vestibular disturbance. No other neurologic changes were disclosed. The patient was extremely euphoric.

The average cell count of the spinal fluid (three determinations) was 2⅔ per cubic millimeter; the globulin was 1 and the albumin 13 [8a] (Bisgaard's nitric acid method); the sedimentation rate was 4 mm. in one hour; the serologic reactions for syphilis were negative.

During the first month after discharge the patient recovered completely, and he felt well until September, 1948, when diplopia insidiously developed. This complaint persisted, with varying severity, for a couple of months but had completely disappeared in November, 1948. At this time, after he had been working in cold weather, weakness of the right side of the face of peripheral type suddenly developed, accompanied by diplopia as a consequence of right lateral rectus

6. Brock, S., and Dyke, C. G.: Venous and Arteriovenous Angiomas of Brain: Clinical and Roentgenographic Study of 8 Cases, Bull. Neurol. Inst. New York, **2**:247, 1932.

7. Leyser, E.: Ein Angiom der Brücke, Monatsschr. Psychiat. u. Neurol. **51**:83, 1922.

8. Manuelidis, E. E.: Über Hämangiome des Gehirns, Arch. Psychiat. **184**:601, 1950.

8a. Bisgaard albumin 1 is about 4.6 mg. per 100 cc.

paralysis, and by anesthesia of the right half of the face. The anesthesia disappeared in a fortnight; the facial weakness cleared in a month, and the lateral rectus paralysis improved to some degree but was still present when, on March 14, 1949, he entered the Department of Neurology of the County and City Hospital, Odense, where he stayed for nine days. A tentative diagnosis of basal intracranial arachnoiditis was made.

Examination at this hospital revealed bilateral paralysis of the lateral rectus muscle, slight paresis of the right orbicularis oculi, and slightly reduced action of the left facial nerve in emotional expressions. Pointing tests and finger-to-nose tests were carried out somewhat tremulously; the gait was perhaps slightly ataxic. Ophthalmoscopic and acoustic-vestibular examinations showed a normal condition. The spinal fluid was under a pressure of 120 mm. of water; the Queckenstedt test showed a pressure of 220 mm.; the average cell count was 4⅔ per cubic millimeter (three determinations); the globulin was 0 and the albumin 12 (Bisgaard method). Roentgenograms of the skull showed nothing abnormal. With the unipolar lead, the electroencephalogram showed some change in frequency, with a dominating activity at 10 to 11 Hertzian waves; with the bipolar lead the record showed nothing abnormal. The Wassermann reaction of the blood was negative; the sedimentation rate was 3 mm. in one hour. Mentally the patient was agile and erethistic.

At follow-up examination, three months after discharge, the diplopia was unchanged, but otherwise there was no complaint. Bilateral abducens paralysis was present; there was slight tremulousness in performing the finger-nose test, with greater ataxia on the right side than on the left.

The patient was readmitted on Nov. 13, 1950. He had been able to work until the day before admission; but, owing to the diplopia, he had constantly worn a patch before the right eye. For some time he had had pain in the right side of the nape of the neck, and the day before admission he felt ill. At 2 a. m. disturbances of speech were noticed. On admission, he was awake, but his speech was slurred. Bilateral lateral rectus paralysis and paralysis of the right orbicularis oculi and zygomaticus were present. The deep reflexes of the extremities were exaggerated, but there was no Babinski sign or paralysis of the frontalis muscle, the muscles of mastication, the soft palate, or the tongue. One hour after admission he suddenly became unconscious for a short period. The next morning he again became unconscious, with transitory cessation of respiration; and in the afternoon he had another attack of cessation of respiration. He had several attacks in which he vomited copious quantities of sanguineous matter, and the temperature rose to 40 C. (104 F.). He died on Nov. 15, in an attack of choking. Laboratory studies (Nov. 15) showed bloody spinal fluid, an average cell count of 22 per cubic millimeter (three determinations); 63,000 red blood cells per cubic millimeter; globulin 1 and albumin 20 (Bisgaard method), and a sedimentation rate 2 mm. in one hour. The diagnosis was uncertain; a tentative one of angioma of the pons was made.

Epicrisis.—From the age of 36 until his death, four years later, the patient, who had previously been healthy, had intermittent symptoms of disturbance of a number of cranial nerves, viz., the right trigeminus, the abducens on both sides (pontine ocular paralysis), the right facial and, possibly, the acoustic and glossopharyngeal nerves on both sides. Slight transitory sensory symptoms were present in the form of dysesthesia on the right side and bilateral finger paresthesias, but there were no signs of infection or of increased intracranial pressure. In the terminal phase of the disease blood was disclosed in the spinal fluid.

Autopsy.—The organs of the thorax and the abdomen were found to be congested, and far-advanced autolysis was present; this had produced a perforation of the stomach. Gastric contents were present in the abdominal cavity, but there were no signs of intravital reactions to this lesion. Postmortem examination of the trunk was otherwise noncontributory, but in the brain a lesion resembling an extensive hemorrhage was disclosed. The lesion affected the caudal three-fourths of the pons, being sharply delimited toward the medulla oblongata and in the most severely affected area leaving only a rim, 2 mm. wide, of intact brain tissue. The lesion was without connection with the meninges, the latter revealing no changes or vascular abnormalities.

Histologic Examination (Henning Wolthers): Horizontal sections of the pons revealed a tumor-like lesion, accompanied by hemorrhage, which also was space-taking. The hemorrhage had caused infiltration of blood into and degeneration of the brain tissue, with incipient resorption

in several places; in the latter areas numerous characteristic fat-resorbing microglial cells were observed. This finding suggests that the hemorrhage had occurred intermittently over a period of several days, so that resorption had already begun in the areas first affected. The tumor had the structure of an angioma, with closely packed, extremely thin-walled, dilated, irregular, abnormal vessels, the lumina of which showed great variation in form and size. The vessel walls consisted merely of endothelium resting on a thin layer of connective tissue. In characteristic areas the stroma was sparse and hypocellular; it stained like connective tissue and did not contain remnants of cerebral parenchyma. In the peripheral areas abnormal vessels were seen, lying singly or in groups in the parenchyma.

The angioma was irregular in shape, with interspersed areas of normal brain tissue. Both in the stroma of the tumor and in the surrounding brain tissue were signs of old hemorrhages, with macrophages laden with blood pigment and sclerosing connective tissue or reparative gliosis, even though the latter was difficult to recognize, owing to the poor stainability (autolysis) and the blurring of the structures.

Fig. 1 (Case 1).—Marginal zone of angioma. Large loops of veins present very thin walls. Inside angiomatous area are widespread hemorrhages.

CASE 2.—A woman, born in 1894, had in 1941 a sudden attack of weakness in the left hand and leg, nausea, headache, vomiting, and diplopia. She was confined to bed for a couple of days, but the paralysis and the diplopia did not completely disappear until about six months later.

On Dec. 19, 1943, loss of power again developed, this time in the right arm and leg. The attack began with malaise, headache, and vomiting, after which the weakness gradually developed. Speech was affected from the onset. The patient entered the State Department of Neurology of Aarhus City Hospital on Dec. 30, 1943. The loss of power had increased; the speech disturbances had been aggravated, and impairment of vision and diplopia had developed. The patient wore spectacles, with a frosted glass before the right eye. She had difficulty in urination. On clinical examination only slight speech disturbance was noted. The ophthalmoscopic examination showed a normal condition. Ptosis was present, bilaterally, notably on the right side. The pupils were of equal size; the response to light was normal, while no reaction could be elicited in accommodation. The right eye showed a slight outward deviation and could not be moved horizontally. There was weakness of the left side of the face of peripheral type. There was weakness of the masseter, and the jaw deviated to the left. The left cornea was anesthetic. The abdominal reflexes were absent. Power in the right arm was reduced, notably in the distal

muscle groups; there was no definite increase in muscular tone or disturbance in deep reflexes. There were marked ataxia and intention tremor of the right arm (in the finger-nose test) and slight ataxia of the left arm. The position and stereognostic senses in the right arm were abolished. Mild loss of power of flexion and extention was noted in the right hip. The position sense in the right foot was greatly impaired. The knee-heel test showed tremulousness on both sides. The Babinski sign was not elicited.

The next day the condition was unchanged except for a Babinski sign on the left and a questionable plantar reflex on the right. On Jan. 2 pneumonia developed, and the patient died on Jan. 3. The Wassermann reaction of the blood was negative; the sedimentation rate was 2 mm. in one hour. The spinal fluid was not examined.

A diagnosis of pontine encephalitis and bilateral bronchopneumonia was made.

Autopsy.—Confluent bronchopneumonic foci were found in both lungs. The surface and sections of the brain did not show any abnormalities. Horizontal sections of the pons and cerebellum disclosed a hemorrhage in the posterior part of the pons; it extended posteriorly, at the same time compressing and dilating the entire fourth ventricle. A rim of pontine tissue was present between the hemorrhage and the wall of the fourth ventricle. The size of the hemorrhage was that of a large hazelnut. Anteriorly, on the right side of the pons, a hemorrhage, the size of a pea, surrounded by several smaller hemorrhages, was observed; it extended into the upper part of the medulla oblongata.

Fig. 2 (Case 2).—Gross appearance of angioma in pons.

Histologic Examination: The angioma consisted of irregularly dilated, convoluted vessels, varying greatly in size. Proliferation of connective tissue was seen, notably in the walls of the larger vessels, where these were not destroyed by the hemorrhage. Between the various parts of the angioma normal parenchyma was seen, in which some larger and smaller hemorrhages had occurred. The glial cells contained hemosiderin.

In a few places patchy accumulations of newly formed capillaries were seen.

The histologic diagnosis (Munch-Petersen) was telangiectases of the pons.

Case 3.—A man, born in 1865, had been healthy up to Christmas time, 1946. He had never suffered from any serious illnesses. On Dec. 19, 1946, he was admitted to the Neurological Department of Frederiksberg Hospital, after having sustained an injury to the head in falling from his bed. He was extremely senile, and his memory was greatly impaired. A roentgenogram of the skull revealed arteriosclerosis. Owing to progressive senile dementia, he was transferred to the psychiatric department on Aug. 2, 1947. He was then deteriorated, disorientated, and uncleanly. On Nov. 7 he was transferred to the Mental Hospital at Oringe, where he died three weeks later, in hyperpyrexia. No neurologic focal symptoms had been observed, and the diagnosis was senile dementia.

Autopsy.—Postmortem examination disclosed pneumonia with wet pleurisy in the right lung, sclerosis of the aorta and coronary arteries, bilateral nephrosclerosis, and adenomatous hypertrophy of the prostate. Hemorrhages were present in the stomach and the rectovesical pouch.

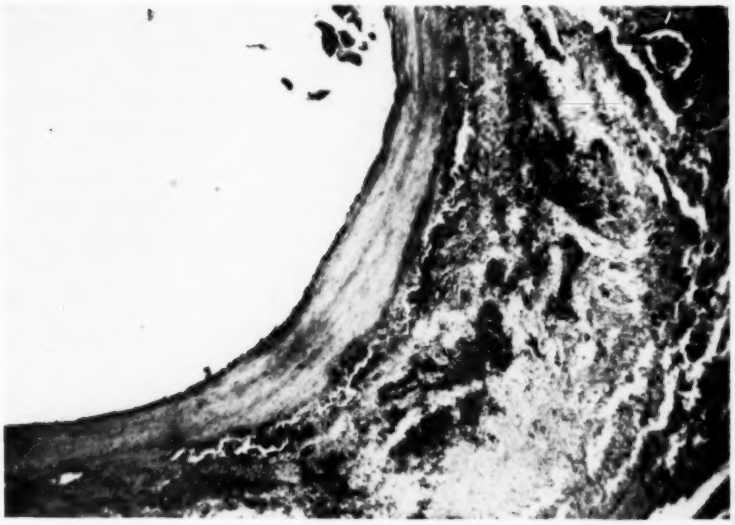

Fig. 3 (Case 2).—Vessel wall of large vein with hyalinization and sclerosis. Around the vessel is pronounced proliferation of connective tissue with edematous, necrotic brain parenchyma.

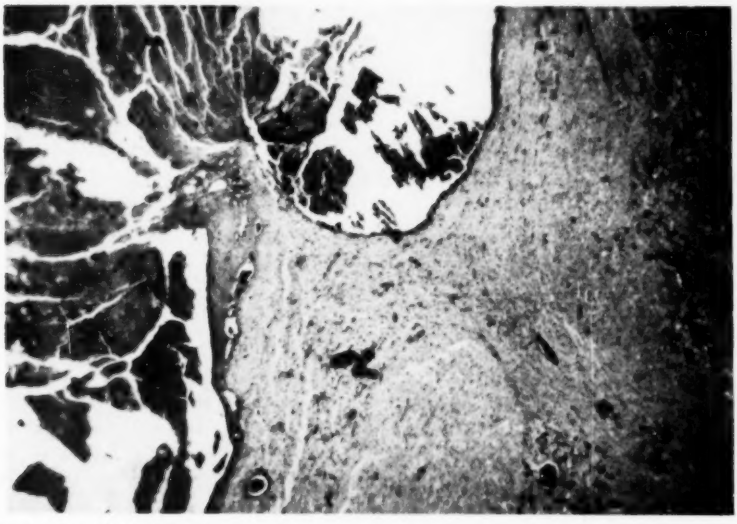

Fig. 4 (Case 2)).—Marginal zone of angioma. The vessel walls consist of a thin endothelial membrane.

The brain, which was well preserved, was fixed in formalin. Examination revealed pronounced cortical atrophy of both frontal lobes and moderate atrophy of the temporal lobes. In these regions there were pronounced sclerosis of the meningeal vessels and thickening of the leptomeninges. On the base of the brain far-advanced sclerosis of the larger arteries and mild thickening of the meninges were noted. The ventricular system was diffusely dilated, and in the pons a hemorrhagic infarct, the size of a hazelnut, was found.

Except for atrophic and sclerotic processes, the microscopic examination disclosed nothing of interest except in the pons, the infarction of which appeared to be a hemangioma, about 1.5 cm. in diameter. Its histologic structure is described as follows:

Microscopic Examination of Angioma of Basal Part of Pons (Institute of Brain Pathology): The tumor tissue was made up of very thin-walled vessels, of slightly varying diameter. The walls of most of the vessels were composed of typical endothelial cells lining a very fine membrane of connective tissue fibrils. In a few places the walls were slightly thicker, owing to hyalinization of the membrane. Nowhere could smooth muscle cells be demonstrated.

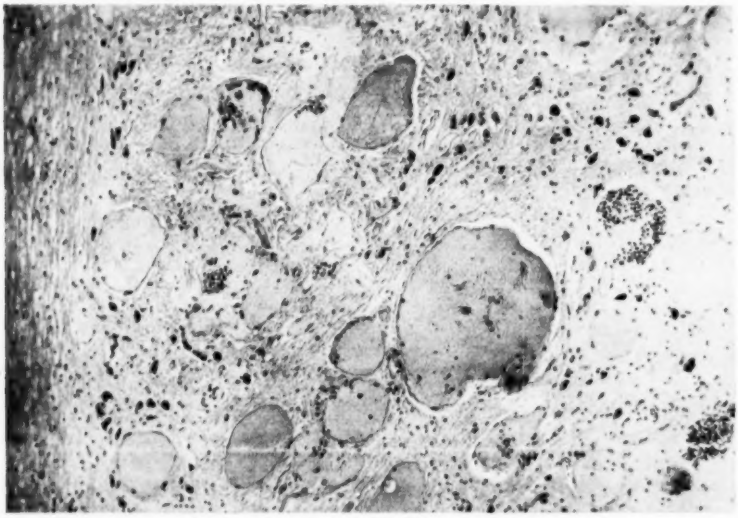

Fig. 5 (Case 3).—Telangiectases of the pons. Among the thin-walled vessels normal architecture of the pons is recognizable.

In some areas the loops of the vessels were lying close together, while in other areas brain tissue separated the lumina of the vessels. However, even in the denser areas both glial and nerve cells were present in the intervascular tissue, so that the structure of the pons was grossly intact. There was no increase in the glia around the vessels, but some of the glia cells contained small quantities of a brownish pigment, which did not, however, resemble blood pigment.

It was astonishing to note that many of the nerve cells in the nuclei pontis within the angioma contained as much melanotic pigment as is usually found in the substantia nigra of the mesencephalon. Otherwise, the nerve cells did not appear abnormal.

The histologic diagnosis was telangiectases of the pons (K. A. Lorentzen).

COMMENT

Three cases of hemangioma of the pons are reported. Histologically, one was a case of cavernous hemangioma, and the two others, cases of telangiectases of the pons.

Clinically and symptomatically, the lesions in Cases 1 and 2 differed greatly from that in Case 3. The latter must be designated as an incidental postmortem finding, which apparently had never produced any symptoms.

In the first two cases reported symptoms of pontine disorder were presented. In Case 1 the fifth, sixth, and, possibly, the eighth and ninth, cranial nerves, and in Case 2 the third, fifth, sixth, seventh, and, possibly, the ninth cranial nerves, were affected. In addition, signs of a lesion of the bulbar paths were evident in both cases.

The duration of the disease was four years in Case 1 and slightly more than two years in Case 2. In both cases the symptoms seemed to have been related to hemorrhages from the angioma; the course was intermittent, with subacute symptoms, which gradually subsided until partial or complete recovery was attained. In neither case were choked disks encountered; i. e., there were no signs of increased intracranial pressure. The spinal fluid did not reveal any evidence in favor of the assumption of intracranial hemorrhage. However, in Case 1 bloody spinal fluid was found immediately before death, indicating that the hemorrhage had forced its way into the subarachnoid space. The sedimentation rate was not increased, and the temperature did not suggest the presence of an infectious process. In Case 1 the temperature had been normal during all previous admissions and was raised only in the final stage of the disease, on the last admission. In Case 2 the temperature was recorded only shortly before death and was then found raised; this is a common finding with cerebral hemorrhages and cannot be taken as supporting a diagnosis of infection.

PREVIOUS INVESTIGATIONS

The literature on the subject consists largely of reports of cases, appearing in a large number of periodicals. In a critical review of these reports some cases have had to be excluded because the available information was too uncertain, but a total of 42 cases remains which may with certainty be regarded as instances of hemangiomas, even though the finer histologic composition is not always described in sufficient detail to allow of a closer classification. The first case was reported by the founder of cellular pathology, Virchow, who took a great interest in vascular tumors.

In the accompanying Table these 42 cases from the literature are arranged in chronological order according to the year of publication. At the end of the Table I have placed the three cases reported in this paper. In the comments on the Table, the histologic place within the classification of Manuelidis is discussed, and the clinical symptoms are noted.

Comments on Table.—Case 1.—It seems fairly reasonable to classify Virchow's case [2b] as one of telangiectases, even though it does not definitely so appear from the description.

Case 2.—Creite [9] found a total of eight cases of angiomas, including one of the pons. The histologic diagnoses were not unquestionable. He reported that cavernous spaces with a strongly developed elastic membrane were observed. Brain tissue and connective tissue were present between the individual spaces, and the case may reasonably be supposed to have been one of venous hemangioma. The angioma of the pons was not, unfortunately, subjected to microscopic examination, but it was probably of the same structure as the six tumors examined.

Case 3.—As judged from the description, Nambu's [10] case is undoubtedly one of cavernous hemangioma.

9. Creite: Zur Pathogenese der Epilepsie: Multiple Angiome des Gehirns mit Ossifikation, München. med. Wchnschr. **50**:1767, 1903.

10. Nambu, T.: Hämangiom im Pons Varoli, Neurol. Centralbl. **26**:1162, 1907.

Summary of Cases of Hemangioma of the Pons

Case No.	Author	Year of Publication	Age at Death, Yr.	Sex	Diagnosis	Multiple Tumors	Pontine Symptoms from Tumor	Duration of Symptoms from Tumor	General Brain Symptoms
1	Virchow [20]	1851	..	F	Telangiectases (?)	..	—	.....	—
2	Creite [9]	1883	21	F	Hemangioma venosum (?)	+	—	.....	—
3	Nambu [10]	1907	63	M	Hemangioma cavernosum	..	?	.....	?
4	Enders [11]	1908	60	F	Hemangioma cavernosum	..	?	.....	+ Epilepsy
5	Clingestein [12]	1908	50	M	Telangiectasis (?)	..	—	.....	+ Epilepsy
6	Claude and Loyez [13]	1911	68	M	Telangiectasis	+	—	.....	+ Hemiplegia
7	Lafora [14]	1911	63	M	Hemangioma cavernosum (?)	..	—	.....	+ Psychosis
8	Lafora [15]	1912	22	F	Hemangioma arteriovenosum	..	?	.....	+ Psychosis
9	Sommerfelt [16]	1919	57	F	Telangiectasis (?)	..	—	.....	—
10	Leyser [7]	1922	20	F	Hemangioma arteriovenosum	..	+	20 days	—
11	Malamud [17] Jakob [21]	1925	51	F	Hemangioma venosum (?)	+	+	13 yr.	+ Psychosis
12	Marcus [22] Bergstrand and others [4]	1925 1936	32	F	Telangiectasis	..	+	1 yr.	—
13	Berger and Guleke [23]	1927	25	M	Hemangioma cavernosum (?)	+	+	2 mo.	—
14	Pinéas [24]	1927	23	F	Hemangioma cavernosum	..	+	5 (13?) yr.	—
15	Kufs [25]	1928	81	M	Hemangioma cavernosum	..	—	.....	+ Dementia senilis
16	Cushing and Bailey [3]	1928	33	F	Telangiectasis	..	—	.....	+ Loss of consciousness
17	Nalin [26]	1928	11	?	Hemangioma cavernosum (?)	..	+	9 mo.	+ Loss of consciousness
18	Schley [29]	1928	58-72	M	Telangiectasis	..	—	.....	—
19	Schley [29]	1928		M	Telangiectasis	..	—	.....	—
20	Schley [29]	1928		M	Telangiectasis	..	—	.....	—
21	Schley [29]	1928		F	Telangiectasis	..	—	.....	—
22	Roussy and Oberling [30]	1930	63	M	Hemangioma cavernosum	..	—	.....	—
23	Michael and Levine [31]	1936	8	F	Telangiectasis	+	+	4 mo.	—
24	Davison and Rosenbeck [32]	1937	58	F	Telangiectasis	+	+	?	+ Psychosis
25	Courville [33]	1937	70	M	Hemangioma cavernosum (?)	..	—	.....	+ Psychosis
26	Jentzer [34]	1938	57	M	?	..	+	3 mo.	—
27	Sjövall and Lundgren [5]	1938	56	F	Telangiectasis	+	?	.....	+ neurologic symptoms
28	Sjövall and Lundgren [5]	1938	28	M	Telangiectasis	+	+	12 days	—
29	Zeldenrust [35]	1938	29	F	Hemangioma cavernosum	+	+	3 days	—
30	Richardson and Bagnall [36]	1940	23	M	Hemangioma arteriovenosum	..	+	16 yr.	—
31	Antoni [37]	1941	35	M	Telangiectasis (?)	..	+	6 yr.	—
32	Antoni [37]	1941	41	M	Telangiectasis (?) Hemangioma venosum (?)	.. ..	+	11 mo.	—
33	Neuhuerger and Silcott [38]	1941	45	F	Telangiectasis	..	—	.....	+ Encephalopathia
34	Neuhuerger and Silcott [38]	1941	42	F	Telangiectasis	..	—	.....	+ embolism aa. cerebri
35	Altschul [39]	1945	19	M	Telangiectasis	..	—	.....	+ Epilepsy
36	Kaufmann [40]	1949	24	M	Hemangioma cavernosum	+	+	2 mo.	+ Epilepsy
37	Manuelidis [8]	1950	39	F	Telangiectasis	..	—	.....	+ Psychosis
38	Manuelidis [8]	1950	24	M	Hemangioma cavernosum	..	?	.....	+ cerebral palsy
39	Manuelidis [8]	1950	70	M	Hemangioma cavernosum	..	—	.....	—
40	Manuelidis [8]	1950	49	F	Hemangioma cavernosum	..	?	.....	+ Wilson's pseudosclerosis
41	Bergman [41]	1950	8	M	Hemangioma arteriovenosum	..	+	5 yr.	—
42	Grotts [42]	1950	2	F	Hemangioma cavernosum	..	+	2 days	—
43	Teilmann	1952	40	M	Hemangioma cavernosum	..	+	4 yr.	—
44	Teilmann	1952	49	F	Telangiectasis	..	+	2 yr.	—
45	Teilmann	1952	82	M	Telangiectasis	..	—	.....	+ dementia senilis

CASE 4.—As Enders [11] reported that no glia, but only a sparse amount of connective tissue, was present between the vessel loops in his case, I have classified it as one of cavernous hemangioma. However, I am not convinced of the correctness of the interpretation, notably because the presence of arterial vessels was reported, for which reason the proper diagnosis may have been one of arteriovenous hemangioma. It is difficult with certainty to rule out focal symptoms, but in all probability the right-sided convulsions, which were of the Jacksonian type, were unrelated to the angioma.

CASE 5.—Clingestein [12] did not expressly mention the presence of nerve and glial tissue between the individual lumina of the vessels; but as he expressed the opinion that the case was one of telangiectases, this diagnosis has been retained.

CASE 6.—It cannot be doubted that the case reported by Claude and Loyez [13] was one of typical telangiectasis.

CASE 7.—Lafora's first case [14] was presumably one of cavernous hemangioma. He stated: "A spot was found . . . which was full of very dilated vessels almost in contact with each other and some few lymphocytes between them; . . . the structure of this was of a small angioma." The structure of the walls of the vessels was not described.

CASE 8.—Lafora's second case [15] must be supposed to have been one of arteriovenous hemangioma. It is not clear whether or not focal symptoms were present. The pupils were stiff, the left being smaller than the right. The angioma could not have been the cause of the patient's psychotic symptoms.

CASE 9.—Sommerfelt's [16] case is available only in abstract. It seems to have been one of telangiectases, but a venous hemangioma cannot be ruled out.

CASE 10.—Leyser [7] reported that only six previous cases had been published, including three in the German literature. The latter three are those reported by Nambu, Enders, and Clingestein. Concerning the cases published elsewhere, Leyser referred to Chabrol.[17] The latter, however, did not personally report cases of angioma of the pons but cited Joseph [18] in whose case the lesion was localized not to the pons but to the medulla oblongata, and to Switalski, whose paper I have been unable to find on the basis of the scant information cited by Chabrol. Leyser's own case must presumably be interpreted as an arteriovenous hemangioma, but he emphasized that in some places the vessels lay so close together that there was no tissue between them. Leyser said that these areas of the lesion should be called *Hämangioma simplex*, but this term is otherwise used to refer only to the telangiectases, which are characterized by the presence of nerve and glial tissue between the vessels. It seems more likely that in these places the tumor was of a cavernous structure, which has, incidentally, been found in several cases.

CASE 11.—The case described by Malamud [19] was presumably one of venous hemangioma. It formed a direct continuation of the dilated veins observed on the floor of the fourth ventricle, and the description of the vessel walls is also suggestive of veins. However, in some areas

11. Enders: Ein Angiom in der Brückengegend, München med. Wchnschr. **55**:1646, 1908.

12. Clingestein, O.: Zur Symptomatologie der Ponserkrankungen, Inaugural Dissertation, Würzburg, 1908.

13. Claude, H., and Loyez, M.: Sur certaines angiectasies capillaires des centres nerveux, Rev. neurol. **19**:64, 1911.

14. Lafora, G. R.: Obscure Symptomatology with Tumors of Fourth Ventricle with Report of Case of Ependymoglioma of Fourth Ventricle Associated with Angioma of Pons, New York M. J. **94**:1027, 1911.

15. Lafora, G. R.: Angioma of Pons: A Consideration of Tumors of the Brain, New York M. J. **96**:1007, 1912.

16. Sommerfelt, L.: Forhandlinger i det medicinske Selskap, Kristiania 1919, Kristiania, Norway, 1920, p. 62.

17. Chabrol, E.: Les tumeurs du bulbe, Encéphale **3**:403, 1908.

18. Joseph, M.: Über Geschwülste des vierten Ventrikels, Ztschr. klin. Med. **16**:349, 1889.

19. Malamud, W.: Über einen Fall von multiplem Hämangiom des Zentralnervensystems, Ztschr. ges. Neurol. u. Psychiat. **97**:651, 1925.

the tumor showed a more cavernous structure. In Dandy's [20] survey both this case and one reported by Jakob [21] are included. However, a closer study reveals that these two cases in reality are one and the same. This is astonishing, since almost all characteristics reported of the two cases are described differently. It should be said that this confusion is not due to either Malamud or Jakob, but, rather, to Dandy's review of the papers of these authors. The description by Malamud was better and more detailed than that by Jakob, who stated that a more detailed report would follow.

Bergman stated that the role played by the angioma in the clinical picture of Malamud's case was uncertain, but I do not agree with him on this point. Microscopically, signs of previous hemorrhages were found in the pons, and this finding is consistent with the clinical picture, in which intermittent symptoms from lesions of pontine nuclei and pathways were observed.

Case 12.—This case was originally published by Marcus [22] in 1925 under the diagnosis of cavernous angioma, but the author did not give a detailed description of the histologic picture. In 1936, Bergstrand and associates [4] published a histologic report of the case. As judged from this, it cannot be doubted that the case was one of typical telangiectasis. Bergman included Bergstrand's case in a group of cases with insufficient clinical data, because, as he said, Bergstrand stated only that there were progressive "nervous symptoms." However, Bergstrand's expression *Nervensymptome* must be taken to mean "neurologic symptoms," which are disclosed by a closer study of the detailed clinical description published by Marcus, who mentioned a number of pontine focal symptoms.

Case 13.—Unfortunately, Berger and Guleke [23] did not publish a histologic report of their case but merely stated that the lesion was a cavernous angioma. In view of the confusion in terminology, one would seem justified in doubting this diagnosis.

Case 14.—As judged both from the illustrations and from the histologic description, Pinéas' [24] case was unquestionably one of cavernous hemangioma.

Clinically, the case is interesting in that the author, after having seen photographs of the patient at the ages of 10 and 16 years, expressed the view that even at this age she must have had clinical focal symptoms.

Case 15.—Kufs's [25] histologic description clearly shows that the case was one of cavernous hemangioma.

Case 16.—Cushing and Bailey [3] did not present a detailed histologic description, but it can scarcely be doubted that their case was one of telangiectasis, *inter alia*, because they illustrate this section of the study with a picture from Schley's paper showing a typical telangiectasis. The peculiar clinical course of this case can scarcely be related to the angioma. Cushing and Bailey stated that similar pontine telangiectases had been described, for example, by Ohlmacher [26] and Wirgman.[27] In Ohlmacher's case three angiomas were localized in the callosal gyrus, the optic thalamus, and the spinal cord, whereas in Wirgman's case the angioma was situated in the cerebellar peduncle, incidentally associated with a cyst of the cerebellar hemisphere. Thus, these cases do not seem to have been of pontine angioma, for which reason I have omitted them in this survey.

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20. Dandy, W. E.: Venous Abnormalities and Angiomas of Brain, Arch. Surg. **17**:715, 1928.

21. Jakob, A.: Über einen seltenen Fall von multiplem Hämangiom des Centralnervensystems, Zentralbl. ges. Neurol. u. Psychiat. **40**:118, 1925.

22. Marcus: Tumorsymptome bei einigen Erkrankungen im Pons- und Oblongata-Gebiete, Folia neuropath. Est. **3**:433, 1925.

23. Berger, H., and Guleke: Über Hirntumoren und ihre operative Behandlung, Deutsch. Ztschr. Chir. **203**:104, 1927.

24. Pinéas, H.: Klinischer und anatomischer Befund eines Falles von Hämangioma cavernosum cerebri ungewöhnlicher Lokalisation und Grösse, Ztschr. ges. Neurol. u. Psychiat. **110**: 281, 1927.

25. Kufs, H.: Über heredofamiliäre Angiomatose des Gehirns und der Retina, Ztschr. ges. Neurol. u. Psychiat. **113**:651, 1928.

26. Ohlmacher: J. Nerv. & Ment. Dis. **26**:395, 1899.

27. Wirgman, C. W.: Angeioma in Cerebellar Peduncle, Lancet **1**:1746, 1914.

CASE 17.—Nalin's [28] case is rather doubtful. The original paper was unavailable to me, and in Wexberg's abstract it was stated that the fourth ventricle was filled by a tumor extending deep into the pons, from which it was sharply delineated. Possibly the tumor only compressed the pons but did not arise from it. In his survey, Dandy [20] mentioned a case in which the tumor was localized on the pons and medulla. This tumor communicated with the pons only through a single vein, while it was connected with the medulla oblongata and the spinal cord through two other veins. Accordingly, Dandy's case has not been included in this survey.

CASES 18-21.[29]—The telangiectases were incidentally noted at autopsy. They were encountered in the same pathological institute within one year, an incidence strongly suggesting that such telangiectases are far more frequent than would be suspected from the literature. The cases were not described singly, but it appears from Schley's collective description that while three of these cases were of common telangiectases, the fourth represented a transitional form to cavernous hemangioma. Bergman classified Schley's case in the group with insufficient clinical data but seems to have overlooked Schley's express statement that in none of the cases had the tumor produced clinical symptoms.

CASE 22.—Roussy and Oberling [30] reported that their case was one of a cavernous angioma the size of a cherry stone. They did not expressly state whether or not brain or glial tissue was present between the individual vessels, but the illustration seems to show a cavernous hemangioma. It is difficult to distinguish the structure of the vessel walls.

CASE 23.—In Michael and Levine's [31] case it cannot be doubted that the lesion was of the nature of telangiectasis.

CASE 24.—Davison and Rosenheck's [32] case, for which the accompanying illustration is very instructive, is similar to Michael and Levine's.

CASE 25.—Unfortunately, I have been unable to obtain Courville's [33] paper. Bergman, who cited the case, did not give a detailed histologic description but merely stated that the tumor was a cavernous angioma.

CASE 26.—Jentzer [34] did not give any histologic description of the tumor. The legend under the illustration of the macroscopic specimen says, *hemangiome, maladie de Lindau*, but the paper does not contain evidence in support of a diagnosis of Lindau's disease.

CASES 27-28.—The tumors in Sjövall and Lundgren's [5] two cases were described as typical telangiectases with transitions to cavernous structure in some places. Bergman reported only one of these cases. In the second case it is difficult to assess the full extent of the involvement, but the hemorrhage must have extended throughout the pons. The authors stated that the case illustrates, *inter alia*, the tendency of angiomatous processes to become localized beneath the ependyma and in the pons.

CASE 29.—Zeldenrust's [35] description leaves no room for doubt that his case was one of multiple cavernous angioma.

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28. Nalin, E.: Su di un caso di angioma cavernoso del pavimento del IV° ventriclo, Riv. sper. di freniat. **51**:115, 1927, cited by Wexberg, E.: Zentralbl. ges. Neurol. u. Psychiat. **48**:563, 1928.

29. Schley, W.: Über Hämangiome im Bereich der Brücke, Zentralbl. allg. Path. **41**:337, 1928.

30. Roussy, G., and Oberling, Ch.: Angiomes du type caverneaux, Presse méd. **38**:179, 1930.

31. Michael, J. C., and Levine, P. M.: Multiple Telangiectases of Brain, Arch. Neurol. & Psychiat. **36**:514, 1936.

32. Davison, C., and Rosenheck, C.: Telangiectases of Brain Stem Associated with Obstructive Hydrocephalus and Mental Deterioration, New York J. Med. **37**:1909, 1937.

33. Courville: Angioma of Pons: Review of Literature and Report of Case, Bull. Los Angeles Neurol. Soc. **2**:78, 1937, cited by Bergman, P. S.: Hemangioma of Pons, J. Mt. Sinai Hosp. **17**:119, 1950.

34. Jentzer, A.: Les tumeurs cérébrales, Helvet. med. acta **5**:721, 1938.

35. Zeldenrust, J.: Case of Angiomatosis Cerebri, Am. J. Cancer **34**:234, 1938.

Case 30.—Richardson and Bagnall [36] diagnosed the lesion in their case as an arterial angioma. Thus they are in agreement with Cushing and Bailey, who, on the basis of clinical findings, designated the tumor as arterial when its presence was indicated by an audible sound. Such a tumor must also communicate with the arterial side of the circulation, a point which neurosurgically is of the greatest importance. In my opinion, Manuelidis justly criticized this point of view, since it is impossible to decide post mortem whether or not arterial blood has passed through a given vascular tumor during life. After death, the histologic structures provide the only reliable criteria. The case under consideration seems to have been one of arteriovenous hemangioma.

Cases 31-32.—The tumors in Antoni's [37] cases 2 and 3 must be classified as telangiectases, even though it does not appear with certainty whether brain substance or glial tisue was present between the individual loops of the vessels. Antoni arrived at the same diagnosis, although he stated that his third case was one of racemose (telangiectatic?) angioma, and it must be admitted that the vessels were strikingly wide (1 to 3 mm.). On the other hand, he emphasized that both the tunica elastica and the tunica muscularis were absent.

Cases 33-34.—Neubuerger and Silcott [38] described the histologic picture in their two cases collectively; even though the vessel walls in some places showed signs of fusion, the tumors may reasonably be classified as telangiectases. Furthermore, there seemed also to be transitions to a venous hemangioma, since large vessels of a vein-like structure were present. The authors described the clinical picture in these two cases. They stated that the histologic composition was representative of three other cases which they had observed within recent years, in which the angiomas had apparently also been localized in the pons. However, as no detailed description is available, I have not included the last three cases in this survey.

Case 35.—Altschul's [39] case was one of telangiectasis, in which, however, venous vessels were also present. Altschul thought that these malformations arise particularly in the gray substance, and he advanced a hypothesis to explain this origin. On the basis of my own and other available material, I am unable to give an opinion on this contention.

Case 36.—In Kaufmann's [40] case it was not expressly pointed out that no brain or glial tissue was present between the loops of the vessels, but the description seems to provide decisive evidence in favor of a diagnosis of cavernous hemangioma, which Kaufmann himself also believed the lesion to be.

Case 37.—Manuelidis [8] distinguished between primary and secondary telangiectasis, the former, in his opinion, being due to a developmental anomaly, while the latter was a phenomenon secondary to circulatory changes, such as thrombosis. In cases of the former type an increased number of vessels should be present, whereas in the latter the anomaly should merely be one of dilatation (both in width and length) of existing vessels. Here, also, I am unable to give an opinion as to this classification. In one of Manuelidis' cases the tumor was a secondary telangiectasis of the pons, and he did not report any primary lesions in this localization.

Cases 38-40.—Manuelidis reported three additional cases of vascular tumors of the pons, viz., Cases 6, 7, and 8. In these three cases the histologic diagnosis was cavernous hemangioma.

Case 41.—Bergman's [41] case must undoubtedly be classified as one of arteriovenous hemangioma, since both arteries and veins were present in the tumor.

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36. Richardson, J. C., and Bagnall, A. W.: Recurrent Subarachnoid Hemorrhage Due to Arterial Angioma of Cerebellum and Brain Stem, Canad. M. A. J. **43**:111, 1940.

37. Antoni, N.: Vier Fälle seltenerer Gefässgeschwülste des Zentralnervensystems, Acta chir. scandinav. **85**:7, 1941.

38. Neubuerger, K., and Silcott, W. L.: Angioma Simplex of Pons, J. Nerv. & Ment. Dis. **94**:586, 1941.

39. Altschul, R.: Hemangioma Pontis, Canad. M. A. J. **53**:465, 1945.

40. Kaufmann, J.: Tumeurs pontines et bulbopontines, Schweiz. Arch. Neurol. u. Psychiat. **64**:197, 1949.

41. Bergman, P. S.: Hemangioma of Pons, J. Mt. Sinai Hosp. **17**:119, 1950.

CASE 42.—Grotts's [42] case was one of cavernous hemangioma. The patient died during the first hemorrhage, which possibly was due to trauma.

Thus, a total of 45 cases of hemangioma of the pons have been found, viz., 17 unquestionable and 4 doubtful cases of telangiectasis, 11 unquestionable and 4 doubtful cases of cavernous hemangioma, 3 doubtful cases of venous hemangioma, and 4 unquestionable cases of arteriovenous angioma. In one case the tumor was either a venous hemangioma or a telangiectasis, and in one case information as to the histologic composition was missing.

SYMPTOMATOLOGY

In 9 of the 45 cases in this survey there were no symptoms of a lesion of the brain or nerves; in 16 there were symptoms of a diffuse lesion of the brain but no, or only very doubtful, focal symptoms. In 4 cases both focal and general symptoms were present, and in 15 cases only focal symptoms were noted. In one case no information as to the symptoms was given.

In 3 of the 16 cases in which general, but not definite focal, symptoms were present, the manifestations were epileptic convulsions. Although some of the authors suggested that such convulsions could be ascribed to the vascular tumors (Schröder van der Kolk,[43] Altschul [39]), it would seem unlikely to assume this as a causal agent, in view of the extremely rare occurrence of epilepsy in cases of infratentorial tumor (Lund [44]). Such considerations also apply to Cushing and Bailey's case, in which fits of loss of consciousness were encountered. In five cases the general symptoms were psychosis; in two, senile dementia, while the following diagnoses were stated in one case each: encephalopathy, embolism of the cerebral arteries, cerebral palsy, Wilson's pseudosclerosis, hemiplegia, and "neurologic symptoms." Only in the last two cases was a causal relation to the angioma probable. Thus, in at least 17, and at most 26, cases the angioma was an incidental finding at necropsy.

From a clinical point of view, the 19 cases with focal symptoms are of special interest (Cases 10, 11, 12, 13, 14, 17, 23, 24, 26, 28, 29, 30, 31, 32, 36, 41, 42, 43, and 44).

A review of the symptoms gives an excellent confirmation of McLean's statement cited in the introduction to this paper. They represent a mixture of nuclear paralyses and pathway lesions, but out of this confusion a diagnosis of pontine lesion may be made in all cases. In 1912 Isenschmid [45] attempted to describe a syndrome characteristic of hemangiomas of the pons, but, in fact, not one of the cases under consideration fits this syndrome, whereas it may apply to a few cases of Lindau's disease. In 1925 Malamud [19] stated that the following symptoms are characteristic of hemangiomas of the central nervous system: persistent pain in the head and at the nape of the neck; localized neurologic and mental symptoms; intermittent disturbances of the optic nerve and other intermittent signs of increased intracranial pressure, such as excitements and apoplectiform paralyses; normal or bloody spinal

42. Grotts, B. F.: Spontaneous Hemorrhage from Hemangioma of Pons, J. Pediat. **37**:98, 1950.

43. Schröder van der Kolk: Over het fijnere zamenstel en de werking van het verlengde ruggemerg, Amsterdam, 1858; cited by Virchow.[2b]

44. Lund, M.: Epilepsy from Intracranial Tumors, Dissertation, Copenhagen, 1952.

45. Isenschmid, R.: Die klinische Symptome des Rankenangioms, München. med. Wchnschr. **59**:243, 1912.

fluid, and, finally, the recurrent and remittent course of the disease. In 1946, in a comprehensive study on the vascular tumors of the central nervous system, Louis-Bar [46] stated that their clinical course is characterized by a long history, with symptom-free intervals. After each attack the patient recovers, but to a less complete degree. This finding, together with the late appearance or complete absence of signs of raised intracranial pressure, should be suggestive of cavernoma or angioma. While Malamud's description seems to fit only a minority of the published cases, a considerable number grossly conform to Louis-Bar's description. However, here we must first exclude all the cases in which the course was very brief, i. e., those in which the patient died during the first attack. Of the cases of symptom-producing tumors included in the present survey, this holds good of Case 10 (20 days), Case 28 (12 days), Case 29 (3 days), and Case 42 (2 days). In the remaining cases the course was more protracted. In some cases there were only two or three attacks; in others, many, so that all degrees were met with, from the cases in which the first hemorrhage from the tumor becomes fatal to cases in which a large number of hemorrhages occur over a period of several years (up to 16), before the fatal one.

The age distribution of the patients at the onset of the first symptoms was as follows: Five were between 2 and 10 years of age; seven, between 18 and 29; three, between 30 and 39; two, between 40 and 49, and two, between 50 and 58 years of age. Thus, the majority of the patients were young persons or children.

If, therefore, intermittent signs of acute or subacute pontine lesion, either without symptoms of increased intracranial pressure or with such symptoms of late onset, and most frequently with incomplete recovery, are encountered in a young person or in a child, the picture is strongly suggestive of a vascular tumor of the pons.

In differential diagnosis a number of conditions must be considered. 1. Encephalitis. Importance should be attached to the absence of an initial febrile phase and, on the whole, to the absence of symptoms suggestive of infection. The intermittent course is often encountered in pontine encephalitis (Stern,[47] with numerous references). 2. Pontine glioma. In this condition a uniform, massive progression is observed. 3. Disseminated sclerosis. Here, the absence of early retrobulbar neuritis and the fact that no focal symptoms develop from new foci during the course are of decisive importance.

TREATMENT

McLean's words "a neurosurgical despair for therapeusis" still hold true with regard to the treatment of these lesions. In some cases operation was performed on the basis of a diagnosis in error, usually that of cerebellar tumor, as in Cases 12, 13, 16, and 30. In the first three of these cases the patient died shortly after the operation, while in the fourth the survival period was six months. Bergman stated that x-ray therapy resulted in an unexpected, marked improvement, but, owing to the remitting course of the disease, it is difficult to evaluate the efficacy of this treatment. That it may have a certain effect on angiomas is more plainly indicated in Cushing and Bailey's Case 8, one of a hemangioma with an arterial communication, which had proved inoperable. After long-continued, intensive radiation therapy, the patient

46. Louis-Bar, D.: Sur les sémiologie et anatomie pathologique de l'angiomatose caverneuse et télangiectasique des centres nerveux, Monatsschr. Psychiat. u. Neurol. **111**:225, 1946.

47. Stern, F.: Epidemische Encephalitis, in Bumke, O., and Foerster, O.: Handbuch der Neurologie, Berlin, Springer-Verlag, Vol. 13, p. 348.

was subjected to a second operation, when it was found that the tumor had been transformed into a mass consisting of indurated, thrombosed, and partially calcified vessels, apparently with only poor blood circulation.

SUMMARY

The classification of the vascular tumors of the central nervous system is discussed. The classification outlined by Manuelidis is found to be the most appropriate. Three cases of hemangioma of the pons are presented; in one of these the angioma was an incidental finding at autopsy, whereas in the remaining two cases the lesions gave rise to definite focal symptoms. The literature on hemangiomas of the pons is reviewed, and the cases are grouped according to Manuelidis' histologic classification. A total of 42 previous cases have been collected, so that the number of known cases is now 45. In nearly half these cases the tumors seem to have been telangiectases; in about a third, cavernous hemangiomas; in about one-half the remainder, venous hemangiomas, and in the other half, arteriovenous hemangiomas.

At least 17, and at most 26, cases represented incidental autopsy findings. In 19 cases focal symptoms were presented; in 4 death occurred during the first attack, but in the remaining 15 cases a characteristic clinical picture was found. The principal features of this picture were as follows: The course was intermittent, with acute or subacute attacks of pontine symptoms; symptoms of increased intracranial pressure were either absent or developed at a late stage of the disease; after each attack the patient recovered, although in most cases incompletely. The disease was most frequent in young persons or children.

X-ray therapy may have a beneficial effect on these tumors.

AGGRESSION, GUILT AND CATAPLEXY

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CATAPLEXY, a symptom of narcolepsy, is an illuminating example of paralysis of voluntary movement induced by emotion. In all the domain of psychosomatic medicine cataplexy is almost without a peer as a compelling illustration of how emotion can give rise, immediately and dramatically, to a physical symptom.

In most of psychosomatic medicine we deal with chronic situations: A man hates his boss and reacts with a peptic ulcer. Cataplexy, in contrast, provides a chance to study acute reactions. Thus, a man may be stricken with paralysis at the moment he raises his hand in anger against his child.

In fully developed narcolepsy there are sleep attacks and paralytic attacks. The latter occur oftenest on emotion and are then called cataplexy. The most striking occurrence is on laughter. On laughing heartily, the patient will collapse in a heap, conscious but unable to move or speak, and will lie helpless for some seconds, or maybe a minute, after which he will suddenly regain his power and be as well as ever.

Earlier students were puzzled by this association of sleepiness (a state that everybody knows intimately) and something so outlandish as cataplexy. Could there be a connection between two symptoms so diverse, one of them a daily and universal phenomenon, the other one something utterly out of the common? That there is a connection is seen in the fact that sleep may be preceded or followed by paralysis. A man falling asleep may suddenly find he cannot move; the paralysis may soon give way to sleep, or, on the other hand, he may become wide-awake again, sleepiness having been dissipated. On the contrary, a man may wake, either from normal sleep or from a narcoleptic nap, with the realization that while he is now awake he is completely powerless. Paralysis while falling asleep (predormitial paralysis) and on waking (postdormitial paralysis) are known collectively as sleep paralysis. Cataplexy and sleep paralysis have this in common, that the victim is powerless while conscious. Indeed, the two states are indistinguishable except on the basis of what has evoked them.

The pathogenesis of narcolepsy would be a complete mystery but for Pavlov's work on cerebral inhibition. The light that his work throws on this problem was discussed in earlier papers,[1] one of which [1k] gives a systematic review of the subject.

1. Levin, M.: (*a*) Cataplexy, Brain **55**:397-405 (Sept.) 1932; (*b*) Pathogenesis of Narcolepsy, with a Consideration of Sleep-Paralysis and Localized Sleep, J. Neurol. & Psychopath. **14**:1-14 (July) 1933; (*c*) Military Aspects of Narcolepsy, with Remarks on the Pathogenesis of Narcolepsy and on Fatigue, ibid. **14**:124-131 (Oct.) 1933; (*d*) "Crowding" of Inhibition and of Excitation, ibid. **14**:345-348 (April) 1934; (*e*) Narcolepsy and the Machine Age: The Recent Increase in the Incidence of Narcolepsy, ibid. **15**:60-64 (July) 1934; (*f*) Role of the Cerebral

The argument therefore need not be restated here in its entirety, and a few points will suffice.

CONDITIONED INHIBITION

Pavlov discovered four methods of producing the inhibition of conditioned reflexes. One of them, conditioned inhibition, is of special importance here.

The animal is trained to expect meat after a stimulus, such as the sounding of a bell. This is done by regularly giving him meat a moment after the bell has sounded. (The giving of meat after bell is called "reinforcement.") When this has been done often enough, the bell becomes a signal which elicits the flow of saliva. The experiment is now modified by combining the stimulus, bell, with another stimulus, say a flash of light, and the combination of stimuli is never reinforced, while the single stimulus, bell alone, is reinforced as always. At first the animal reacts to bell plus light as to bell alone, by salivating. But since bell plus light never brings meat, he learns after a time to differentiate the combination from bell alone, and now the combination will no longer make the mouth water. (Pavlov called bell alone the "positive stimulus," light the "negative stimulus," and the two together the "inhibitory combination.")

Pavlov asked why an animal who at first used to salivate to bell plus light no longer does so. Has the combination of stimuli, since it is not reinforced, lost its former power to evoke excitations in cerebral salivary areas? Or, on the contrary, does it still evoke excitations, which, however, are now held in check, or inhibited? Pavlov found the second alternative to be correct. For example, if the animal, who has already learned not to salivate on bell plus light, is surprised by an alien stimulus given right after the combination (an alien stimulus being one he has never before experienced), the mouth will water. This shows that the excitations were there, and needed only the "disinhibiting" influence of the alien stimulus to be released.

Conditioned inhibition plays a mighty role in adaptation. A response suitable to a given stimulus may be most unsuitable if the situation has been modified by the addition of a special factor. A dog may safely go after a small animal, but not if it has quills. A man may run from danger, but not if he is a soldier under fire.

Relation of Sleep to Inhibition.—Pavlov found that the four methods of producing inhibition may also cause the animal to fall asleep, to a degree varying with the animal. Thus, after a conditioned inhibition has been established, some animals

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Cortex in Narcolepsy: Classification of Narcolepsy and Allied Disorders, ibid. **15**:236-241 (Jan.) 1935; (*g*) Pathogenesis of Cataplexy on Anger, ibid. **16**:140-143 (Oct.) 1935; (*h*) "Crowding" of Excitation as the Immediate Cause of Some Epileptic Fits: Consideration of Pathogenesis of Epileptic Fits Precipitated by Anger and of Those Occurring in Situations of Danger, ibid. **16**:256-260 (Jan.) 1936; (*i*) Morbid Hunger in Relation to Narcolepsy and Epilepsy, J. Nerv. & Ment. Dis. **88**:414-416 (Oct.) 1938; (*j*) Mental Symptoms in Narcolepsy: Forgetfulness and Learning Difficulty as Manifestations of Excessive Inhibition of the Highest Cerebral Centers, Am. J. Psychiat. **98**:673-675 (March) 1942; (*k*) Diplopia in Narcolepsy, Arch. Ophth. **29**:942-955 (June) 1943; (*l*) Military Aspects of Narcolepsy, War Med. **6**:162-165 (Sept.) 1944; (*m*) "Delay" (Pavlov) in Human Physiology: Sleepiness on Delayed Response to Stimuli, Am. J. Psychiat. **102**:483-485 (Jan.) 1946; (*n*) Pathogenesis of Narcoleptic and Epileptic Seizures Occurring Under Acute Emotional Stress, J. Nerv. & Ment. Dis. **111**:101-108 (Feb.) 1950; (*o*) The Sentinel Asleep on Post, Dis. Nerv. System **12**:15-18 (Jan.) 1951; (*p*) Narcolepsy, in The Cyclopedia of Medicine, Surgery and Specialties, Philadelphia, F. A. Davis Company, 1951, Vol. 9, pp. 451-459.

will respond to the inhibitory combination (bell plus light) by falling asleep. The most striking examples of sleep were seen in the experiments on delay.[1m] Pavlov concluded that sleep and internal inhibition are one and the same thing, sleep being inhibition that has irradiated over enough cortex to wipe out consciousness.

Thus, Pavlov was able to induce sleep without using drugs by exposing dogs to situations calling forth the inhibition of conditioned reflexes. This is important in human physiology, for similar situations also induce sleep in man, the soldier under fire being an example. Sleepiness under fire is striking enough, but it is even more so when it appears on the first day at the front line, when the soldier experiences enemy fire for the first time, a moment when one would expect him to break all records for alertness. The soldier is the victim of conditioned inhibition. There is a positive stimulus, the fire, which, if nothing else mattered, would evoke a positive response (he would run away). But there is a powerful negative, or inhibitory, stimulus: He appreciates that he is in a situation where he has to stand fast, whatever the cost. The positive stimulus evokes a motor impulse. The negative stimulus evokes inhibitions that hold the impulse in check. These inhibitions do their job too well. They not only hold the impulse in check, but, overflowing the bounds of motor centers, they spread over the rest of the cortex. Like firemen who may flood a whole building to put out a fire in just one room, inhibitions may inundate the cortex and cause sleep.

The sleepiness of a soldier under fire is but one example of the rule that sleep may occur in any situation in which one suppresses the impulse to escape from danger. Workmen have fallen asleep when exposed to danger, as on a high scaffold, where the impulse to get down must be suppressed because there is a job to be done. Spiller reported the case of a narcoleptic fireman who slept while holding on to the grab irons of a locomotive going 70 miles an hour.

If there is any doubt as to the power of conditioned inhibition to make a man sleepy, it will surely be dispelled by a crucial experiment that nature made for us. A healthy soldier, posted as a sentinel from 2 to 4 a. m., was disappointed at 4 a. m., when the corporal of the guard failed to show up with the expected relief. (The incident took place in the United States; so the man was not exposed to danger.) At first the soldier thought nothing of it, but as the minutes passed it became obvious to him that the corporal had fallen asleep. Unable to leave his post, he resigned himself to waiting, or, rather, he tried to. He walked his post, getting angrier by the minute. He quickly began to feel unbearably tired and sleepy, and it was all he could do to keep his eyes open and drag one foot after the other. He was obsessed with the wish to leave his post and give the corporal a good bawling out, but knew he wouldn't. At last, at 6 a. m., relief came; miraculously, the sleepiness, which a moment before had been overpowering, now vanished as if by magic, and he left his post wide-awake and chipper. This incident is instructive because the sleepiness cleared up so abruptly. Could the fatigue and sleepiness be attributed to overexertion, seeing that the man walked his post the extra two hours? Not at all, for the effects of overexertion do not clear up so quickly; they yield gradually after a substantial period of rest. The soldier was under a conditioned inhibition, since he had to suppress the impulse to leave his post. The moment relief came, conditioned inhibition ceased; he was now free to go, and there no longer was anything to inhibit. The sharp disappearance of sleepiness at that moment, as if by the lifting of a spell, endows this incident with the precision of a laboratory experiment.

The conclusion is reached that circumstances that call forth inhibition may produce sleep, in man as in lower animals. Pavlov found that dogs vary in the ease with which they succumb to inhibition. Just as we speak of excitability, so also may we speak of "inhibitability." The basis of narcolepsy may be said to lie in the undue inhibitability of the cerebral cortex.[1f] (Whether this excessive inhibitability, in turn, depends on some fault of subcortical centers or of some other system, such as the endocrine glands, is another question.) Narcolepsy is thus the physiological opposite of epilepsy, a condition in which the brain, or, to be more exact, one small part of the brain, is unduly excitable.

CATAPLEXY AS A MANIFESTATION OF INHIBITION

Pavlov showed that the cerebral cortex is not static, but that its parts alternate between excitation and inhibition, depending on the stimuli of the moment. He likened the cortex to a mosaic, with areas here and there in a state of excitation, separated by areas of inhibition. Excitation and inhibition oppose each other, like opposing football teams. This struggle explains certain phenomena in man.

Thus, persons prone to narcolepsy report that when they struggle against an impending sleep attack they may suddenly find themselves paralyzed. Sleepiness means that inhibition is irradiating over the cortex, and trying to stay awake means that excitation is called into play to keep it in check. Figuratively, and even literally, one "pinches oneself." The onset of paralysis at this moment shows that inhibition, in process of being halted in its advance over the cortex, may be shunted into motor centers. This shunting reminds one of a football player running with the ball who evades his opponents as they bear down on him and is thus shunted into that part of the field where the opposition is least.

This fact, the occurrence of paralysis on the attempt to ward sleep off, is significant in the light of a phenomenon that has already been mentioned, viz., sleep paralysis. When a man falling asleep finds himself paralyzed (predormitial paralysis), his motor centers have succumbed to inhibition in advance of the rest of the cortex. On the contrary, when it is on waking that he is paralyzed (postdormitial paralysis), the inhibitory spell has been lifted from the rest of the cortex but is still lingering in motor centers, which need a little more time to shake the spell off. These facts, taken together, show that the paralytic attack, like the sleep attack, is an inhibitory phenomenon. Sleep and paralysis are of a piece, and differ only in extent: In sleep it is all, or almost all, of the cortex that lies under the inhibitory spell; in paralysis it is only the motor cortex.

That inhibition is the basis of the paralytic attacks of narcolepsy is supported by a large body of clinical evidence, some of which will be given in this paper. A dramatic and telling example may be given at once. Fabing [2] reported the case of a narcoleptic who became a soldier and went into combat.

> [One night, on guard duty,] he was crouched in a foxhole, and at about 9 p. m. he saw a moving shadow. He challenged the man, but the wind was blowing the wrong way and the man did not hear the challenge. The patient followed the shadow and saw the man step behind the shadow of a tree. He jumped out of his foxhole, put a shell into his rifle and threw the bolt. He was about to squeeze his trigger when the other man said, "Don't shoot, Sleepy; it's Jim." At that the patient went into a heap, and his gun fell from his hands. The other

2. Fabing, H. D.: Narcolepsy, Arch. Neurol. & Psychiat. **54**:367-371 (Nov.-Dec.) 1945; **55**:353-363 (April) 1946.

man rushed forward to see what was the matter. By the time he had crossed the hundred feet of space between them, the patient had regained his motor power.

In this unforgettable example, as in that of the sentinel, already cited, who had to wait until 6 a. m. for relief, the value of the case lies in the dramatic suddenness with which, in a single moment, a reversal of external circumstance caused a revolution in the state of the cerebrum. The two cases are different, for one involved the appearance of inhibition, the other its disappearance. But they are alike in the suddenness and promptness of the response. In the case of the man who had to wait until 6 a. m. the inhibitory signs, fatigue and sleepiness, vanished as if by magic the moment the need to inhibit was abolished by the arrival of relief. In Fabing's case the soldier was about to fire at a man out front when, in the nick of time, he learned the man was on our side, whereupon inhibitions came into play and stayed his hand and he collapsed in a heap.

It is this dramatic suddenness that gives the two examples their meaning. Here are two experiments of nature of such decisiveness and beauty as to strike envy in the heart of the keenest laboratory worker.

CATAPLEXY FROM CONDITIONED INHIBITION; AGGRESSION

Thus far we have seen that (1) when man for whatever reason suppresses an impulse, there is conditioned inhibition; (2) conditioned inhibition may give rise to sleep; (3) the paralytic attacks of narcolepsy are, like sleep, an inhibitory phenomenon. The question now arises: Do these paralytic attacks ever ensue on conditioned inhibition?

Clinical experience gives a clear affirmative answer, for it shows that cataplexy may occur when a man experiences an aggressive impulse that he strives to suppress, or feels he ought to suppress. The major evidence along this line will now be presented.

Cataplexy on Raising the Hand to Strike a Child or Whip an Animal.—In 1935 I [1g] reviewed 11 cases in which cataplexy supervened when the patient raised his hand against his child or his animal. Since then there have been many more cases. The paralysis may be general, affecting the whole body, or only local, affecting the limb that is raised.

These cases reveal the nice balance that can exist between excitation and inhibition. In the motor centers of the angry parent there is a struggle. There are excitations which are about to express themselves in an act of aggression. But there also are inhibitions, for the parent feels guilty and wants to restrain himself. The ancient saw, "This hurts me more than it does you," is far from fantastic, the skepticism of small boys notwithstanding.

Cataplexy may occur in the course of a fist fight. In Cozby's [3] Case 2, the patient, a sailor, was "about to have a fight with a shipmate, [when], at the climax of the quarrel and in the position of readiness to strike a blow, he suddenly found his arm and general body musculature relaxed and powerless . . . The patient stated that as a result, 'I got poked twice in the eye before I could hit back.'"

Negative evidence has its limitations, but one negative instance is important. In a case of narcolepsy reported by Daniels,[4] the patient recalled that he had not

3. Cozby, H. O.: Narcolepsy, with Report of 3 Cases, U. S. Nav. M. Bull. **34**:471-478 (Oct.) 1936.

4. Daniels, L. E.: Narcolepsy, Medicine **13**:1-122 (Feb.) 1934.

been paralyzed when he punished a man who made fun of his infirmity. This was certainly no coincidence. Inhibitions may hinder a man in fighting his fellow, especially in striking a child or an animal, but there is no hindrance in punishing someone who will make fun of a sick man.

Cataplexy may occur also when aggression is merely implicit. Holmes,[5] speaking of a narcoleptic school teacher, said: "Curiously enough, in her case the cataplexy occurred more readily on annoyance than on laughter. She used occasionally to collapse in class if annoyed with a pupil." Even though she did not actually punish the pupil, it's a safe bet that she wanted to.

Coodley [6] reported a case of narcolepsy in which cataplexy occurred when the patient, a wounded but ambulatory soldier in hospital, was teased by his fellow patients. He had gone nine days without a bowel movement, and they were teasing him. He was walking down the ward to the latrine when someone yelled, "Look at him, he looks full in the face." Everybody laughed, and the patient had an attack of cataplexy. Here was a bowel-conscious man, who doubtless felt that after nine days of fruitless effort his constipation was no longer a laughing matter. Moreover, psychoanalysis has shown that bowel function is tied in with personality structure, especially with problems of stubbornness and hostility. Even if the patient took teasing like a good sport, the joke must have awakened a powerful hostile impulse.

In Murphy's [7] Case 7 a woman unhappily married had an attack of cataplexy after an argument with her husband. One day, riding in a store elevator, she was looking over the shoulder of a woman reading a newspaper and "read an account of a man who had been stabbed by his wife and killed. The thought that she might do this entered her mind, and she felt weak and collapsed."

In Case 2 of Wenderowic [8] the patient, a streetcar motor man, had an attack when he was angered by a vehicle on the car track ahead of him. The same author's Case 1 will be cited later.

Ludo van Bogaert [9] reported the case of a man (his Obs. IV) who had his first attack of cataplexy when violently angry.

> He was reprimanding one of his employes; . . . became angry, started to shout, when suddenly his voice changed in quality, he became aphonic, felt a painful constriction in his throat, neck, and shoulders, slowly became weak.

In the case of M. M., in the same paper, cataplexy occurred when the patient got angry at his disobedient nephew and at his dog.

In the case reported by Locke and Bailey [10] cataplexy occurred when the patient tried to chase a neighbor's dog out of her kitchen.

5. Holmes, G., in discussion on Cohen, H.: Proc. Roy. Soc. Med. **21**:1239, 1928.

6. Coodley, A.: Psychodynamic Factors in Narcolepsy and Cataplexy, Psychiatric Quart. **22**:696-717 (Oct.) 1948.

7. Murphy, W. F.: Narcolepsy: A Review and Presentation of 7 Cases, Am. J. Psychiat. **98**:334-399 (Nov.) 1941.

8. Wenderowic, E.: Hypnolepsie (Narcolepsia Gélineau) und ihre Behandlung, Arch. Psychiat. **72**:459-472, 1924-1925.

9. van Bogaert, L.: Les aspects familiaux des paroxysmes réflexes du tonus: Contribution à l'étude des faits de cataplexie et d'hypertonie dites affectives et de leurs relations avec la pathologie constitutionelle, Ann. méd. psychol. **94**(pt. 1):1-27 (Jan.) 1936.

10. Locke, W., and Bailey, A. A.: Narcolepsy: Report of an Unusual Case, Proc. Staff Meet., Mayo Clin. **15**:491-493 (July 31) 1940.

In this matter of conditioned inhibition from a hostile impulse, mention may be made of Case 6 of Thiele and Bernhardt [11]: A narcoleptic soldier had an attack of cataplexy when he "was about to greet" a superior. An airtight case if there ever was one! Incidentally, this man's first attack of cataplexy occurred when he wanted to whip his horse.

There is no need to multiply instances further. The evidence is clear that when a hostile impulse is associated with guilt or shame or fear, paralysis may be the result.

Even when anger is directed against something inanimate, cataplexy may ensue. In Thiele and Bernhardt's Case 33 the patient said: "If I have a parcel in my hand (while walking on the street) and the string breaks, I will collapse."

Adie's [12] Case 3 is a bit different. The patient, a woman of 42, had her first attack of cataplexy "when she heard that a boy who was cycling from London to spend a week-end at her home had been killed on the way; on hearing this news 'all the power went from me' and she sank upon a couch, where she lay powerless, unable to move and unable to say a word."

We are not told whether the patient was a mother, or what she thought on receipt of the bad news. Was she the mother of a lad whom the unlucky youngster was coming to visit? If so, the thought might well have flashed through her mind, "If some one had to die, thank God it was the other boy, and not mine." Soldiers have such thoughts when they see a buddy killed, and the ensuing guilt gives them trouble. There is a difference between the case of this woman and the other cases I have cited. In the other cases an impulse is involved: The patients were about to do something, e. g., to strike a child. Adie's patient, in contrast, if my supposition is correct, suffered merely from a feeling, but a feeling linked to unconscious hostile wishes.

Since acute hostility may provoke cataplexy, it is not surprising that many cases of narcolepsy arise in a setting of chronic hate and resentment. Drake's [13] Case 1 is one in point. The patient was a boy of 13 whose narcolepsy "began one week following the remarriage of his father. The boy openly resented this newcomer to [the] household," and the stepmother reciprocated this hatred. The hate-filled situation reaching a climax with the intrusion of the stepmother, followed only a week later by the onset of narcolepsy—this is an illuminating sequence. Hostility was aroused to the breaking point, necessitating inhibitions which overwhelmed the susceptible youngster.

CATAPLEXY IN HUNTING AND FISHING

In the cases considered thus far, aggression, whether overt or implicit, was serious, in the sense that it was associated with anger or some similar emotion. We turn now to the aggressive impulses of sport and play.

11. Thiele, R., and Bernhardt, H.: Beiträge zur Kenntnis der Narkolepsie: Sonderausgabe von Heft 69 der "Abhandlungen aus der Neurologie, Psychiatrie, Psychologie und ihren Grenzgebieten," Berlin, S. Karger, 1933.

12. Adie, W. J.: Idiopathic Narcolepsy: A Disease Sui Generis, with Remarks on the Mechanism of Sleep, Brain **49**:257-306 (Sept.) 1926.

13. Drake, F. R.: Narcolepsy: Brief Review and Report of Cases, Am. J. M. Sc. **218**:101-114 (July) 1949.

Hunting and fishing provide many examples of cataplexy. A man may succumb when he raises his rifle to fire at game or is about to haul in a fish. Thus, in Fabing's [2] case the patient had his first attack of cataplexy when he was hunting.

> A rabbit came into view and he raised his gun to shoot; but suddenly his arms and neck began to quiver, and, in his own words, "everything gave way under me and I squatted like a wet rag." . . . He had to abandon hunting because as a rabbit jumped up he would lose muscular tone and fall to the ground. . . . He was wading in a shallow creek [one day], "hogging" fish. He grasped a large one, which struggled violently as it broke the surface. This exciting display caused a cataplectic attack. He went limp, sank into the water and lost the fish.

Other examples, in hunting, were reported by Bostock,[14] Cave [15] (Cases 6 and 35), Baxley [16] (Case 1), and Bakst [17]; and, in fishing, by Bostock [18] (Case 2), Cave [15] (Cases 13 and 35), and Speirs and Speirs [19] (Cases 1 and 4).

In Case 1 of Brock and Wiesel [20] it was reported that cataplexy occurred "if [the patient] attempts to scare a cat away, swat a fly, kill a moth or squash a bug . . . He is especially annoyed by his inability to land a fish."

Hunting and fishing involve aggression and guilt. But, you may say, why attribute the cataplexy to these? Cannot it be due simply to the excitement which so notoriously afflicts the hunter when he takes aim or the angler when he feels a nibble? I submit that it is not excitement per se that counts, but the circumstances that attend it. There have been cases of narcolepsy in which the greatest possible excitement has failed to evoke any cataplexy at all. The most striking example was in the case reported by Bostock.[14] This man had cataplexy when he raised his gun to fire at a duck, but not when he tried to stop a runaway horse. There is no lack of excitement when a man tries to stop a runaway horse, but he is not held back by guilt, as he is when he strikes a child or shoots an animal or snares a fish.

CATAPLEXY IN OTHER SPORTS

Boxing.—A remarkable case was reported by Barker.[21] The patient, prior to the onset of his narcolepsy, had done some prize fighting; though he was good, he lost many fights because when he was behind in points, yet had his opponent helpless on the ropes, he "didn't have the heart" to knock him out. He would weep bitterly because he had not been able to unleash the knockout blow. The patient hated his father and had often wanted to knock him down, but, as he later told Barker, "he was my old man." We may assume that the situation in the ring, where he could legitimately knock a man down, was associated in his mind with an illegitimate impulse, the impulse against his father; and the ensuing inhibitions took the steam

14. Bostock, J.: Idiopathic Narcolepsy, M. J. Australia **2**:258 (Aug. 20) 1927.

15. Cave, H. A.: Narcolepsy, Arch. Neurol. & Psychiat. **26**:50-101 (July) 1931.

16. Baxley, H. W.: Narcolepsy, M. Bull. Vet. Admin. **12**:143-148 (Oct.) 1935.

17. Bakst, H. J.: Daily Use of Benzedrine Sulfate over a Period of 9 Years, U. S. Nav. M. Bull. **43**:1228-1231 (Dec.) 1944.

18. Bostock, J.: Idiopathic Narcolepsy, M. J. Australia **2**:239-241 (Aug. 25) 1928.

19. Speirs, G. O., and Speirs, R. E.: Narcolepsy, J. Kansas M. Soc. **38**:54-57 (Feb.) 1937.

20. Brock, S., and Wiesel, B.: Narcoleptic-Cataplectic Syndrome: Excessive and Dissociated Reaction of the Sleep Mechanism and Its Accompanying Mental States, J. Nerv. & Ment. Dis. **94**:700-712 (Dec.) 1941.

21. Barker, W.: Studies in Epilepsy: Personality Pattern; Situational Stress and the Symptoms of Narcolepsy, Psychosom. Med. **10**:193-202 (July-Aug.) 1948.

out of him, so that he "didn't have the heart" to unleash his best punch—a paralysis, like cataplexy, though on a higher level. It is noteworthy that this paralysis of will occurred prior to the onset of the more obvious symptoms of narcolepsy.

Snowballing.—In Case 1 of Speirs and Speirs [19] the first attack of cataplexy occurred when the patient scored a hit in a snowball fight. Despite their enormous quantitative difference, boxing and snowball fighting are of the same essence.

Tennis.—Cataplexy in tennis is so common as to deserve a special place. In the midst of an exciting volley, the racket will fall from the hand, or the arm will become so unsteady as to spoil the return, or the patient will fall down in a full-blown attack.

In boxing, and even (though on a smaller scale) in snowballing, the aim is to hurt your opponent. In tennis there is no such aim, but there may be unconscious impulses. One of the most satisfying experiences in tennis is when you smash the ball right at your opponent, so that he has no time to step aside and make a return, the ball landing somewhere on his body. He is rendered helpless, symbolically killed. The savage triumphant bellow of the player who has thus demolished his opponent is scarcely accounted for by the mere gain of a single point.

Chess.—In Thiele and Bernhardt's [11] Case 11 the patient had an attack of cataplexy in a chess game "when he thought he was going to checkmate his opponent."

Cards.—A winning play at cards may evoke cataplexy. Gélineau,[22] who gave narcolepsy its name, reported (Case *2*) that the patient had an attack when he saw a good play coming up. In Cave's [15] Case 3 the patient noticed in bridge that "he would be all right while losing, but that if he were winning he would 'go all to pieces,' feel weak and be powerless to write the score or shuffle the cards." In Case 1 of Speirs and Speirs [19] the patient had an attack when he made a finesse at bridge, and Coodley's [6] patient when he won a big hand at poker.

Billards.—Palmer's [23] patient had an attack when he made a hard shot at billiards.

When cataplexy occurs in such games as chess, cards, and billiards, in most, if not in all, cases it is when the patient is making a winning play, and not when he is losing. I submit that this is no coincidence. Psychoanalysis has shown that some people confuse aggressiveness and competitiveness with hostility. They feel guilty when they beat a competitor, even in sport, for victory gratifies their unconscious hostile wishes. When they lose a game, they may not like it, but they do not feel guilty. Indeed, losing may assuage their guilt. A winning play, however, fires the hostile impulse and sets the stage for conditioned inhibition and cataplexy.

Chess is a striking example. The prospect of cornering the opposing king does things to a man with an unresolved Oedipus complex. The psychoanalytic implications of chess were discussed in a paper some years ago by Ernest Jones.

Baseball.—Three patients have had cataplexy while playing baseball. There is a striking thing about the cases: Invariably the attack occurred when the patient was about to make a play in the field, and never when he was at bat. In Shapiro's [24] Case *2* the attack occurred when the patient was "attempting to throw the ball into

22. Gélineau: De la narcolepsie, Gaz. hôp., Paris **53**:626, 1880.

23. Palmer, H. A.: Narcolepsy, Brit. M. J. **2**:478 (Oct. 4) 1941.

24. Shapiro, M. J.: Benzedrine in the Treatment of Narcolepsy, Minnesota Med. **20**:28-31 (Jan.) 1937.

the field." In Bakst's [17] case the patient "could catch a ball without difficulty, but could not follow through with the necessary throw." In this case, incidentally, the very first symptom of narcolepsy was an attack of cataplexy in a ball game. In Fabing's case an attack occurred when the patient caught a pop fly. On another occasion, "as he was going into position to tag a runner at third base, he felt an attack of cataplexy coming on. He managed to stop the ball with his glove, but he went down in a heap and dropped the ball."

Is it an accident that cataplexy has never been reported in a batter? I think not. From the standpoint of aggression, there is a difference between batter and fielder. It makes a difference whether aggression is aimed at a group or at an individual; in the latter case the guilt is the greater. When you hit a home run, your aggression is against a team, rather than an individual, except for the unhappy pitcher. In contrast, when you are fielding, your aggression is directed sharply and specifically at an individual. The runner is quick with life until by a good catch or throw, or especially by a tag, you put him out, symbolically killing him.

Football.—In Kinnier Wilson's [25] Case 3 cataplexy occurred when the patient tried to "shoot the ball at goal" in football, which I assume is the game called soccer in the United States. There has been no report of cataplexy in American football. In this game, when a defending player tackles the runner, conditions are ideal to bring out the tackler's susceptibilities to inhibition.

Acting-Out of Aggressive Impulses in Sport.—Play and sport permit the release, in a manner harmless and acceptable, of aggressive impulses that might otherwise prove a burden. A little girl spanks her doll for being bad, thereby doing what she would like to do to her baby sister. The cases that have been cited show that there is more to athletic sports than meets the eye. Innocent fun and sport may serve as the vehicle for the acting out of aggressions which, depending on unconscious feelings and attitudes, may be associated with guilt.

Once more I refer to the valuable case reported by Fabing.[2] As a meticulous case report it is almost in a class by itself, but I cannot share all of Fabing's conclusions. Fabing emphasizes that the patient suffered from cataplexy in many circumstances, but never under artillery fire, and he quotes with approval the patient's explanation of this matter. The patient had said, "Shells never bothered me because I could hear them coming, and that way my nerves could get set for them." But this is the man who had cataplexy when he raised his gun to fire at a rabbit, and when he tried to haul in a fish and to tag a runner coming into third base. He got set then, too, didn't he? A third baseman about to tag a runner is as "set" as anyone could ever be; yet this man had his cataplexy anyway. Whether one has a chance to get set is, therefore, not the crucial factor. We can learn the crucial factor from the dramatic contrast that this case affords. Here is a man cowering under artillery fire, and at this most serious moment of his life he reacts like any other man, but when he is about to shoot a rabbit or pull in a fish or tag a runner his muscles turn to water. Why the difference? I submit it is because in these sports he is about to give vent to aggression, and so there is an upsurge of guilt and of inhibition. He is about to kill—literally as to the rabbit and the fish, and symbolically as to the base runner.

25. Wilson, S. A. K.: The Narcolepsies, Brain **51**:63-109 (March) 1928.

To summarize, when a man is about to give vent to aggressions for which he feels guilty, and which he therefore strives, consciously or unconsciously, to suppress, he may respond with cataplexy. The aggressions may be real and overt, as when he is about to strike his child or beat or kill an animal, or merely implicit, as when he acts out unconscious impulses in tennis or baseball. In either case there is conditioned inhibition, inhibitions coming into play to check the aggressive impulse. Clinical evidence tends to show that when aggression is justified, and hence does not arouse guilt, cataplexy does not occur; a narcoleptic, for example, was able, without let or hindrance, to punish a man who had made fun of his infirmity.

FURTHER PROOF OF THE IMPORTANCE OF AGGRESSION

Of all the precipitants of cataplexy, laughter is the commonest. But aggressive situations are not far behind. The importance of aggression is emphasized by those cases in which cataplexy is evoked by aggression and never by laughter. Thus, in Barker's [21] Case 2 the patient never had cataplexy when he laughed, but only when angry at some member of his family. One attack occurred when he was about to strike his son. In Barker's Case 1 the patient had two degrees of cataplexy. The milder attacks occurred while she was standing and consisted of weakness of the legs, so that the patient fell; these occurred only in laughter. The severer attacks, which involved all the limbs, occurred only when she was angry and "was about to express her emotions in direct aggressive action," especially when she was about to strike her children.

The First Attack.—The importance of aggression is further illustrated by those cases in which aggression gives rise to the first cataplectic attack. Indeed, in some of the cases this first attack of cataplexy was the earliest manifestation of narcolepsy, antedating the first sleep attack. A circumstance that evokes a seizure is important, but it is doubly so when the seizure is the first.

Remarkable in this respect is Case 1 of Wenderowic.[8] Four months after the onset of his sleep attacks the patient had his first cataplectic attack. A farmer, "he was driving his cow from the yard, when he angrily swung his whip at her. At that very moment [he had his first attack of cataplexy]. One week later he had a similar attack when he wanted to whip his horse . . . Next day he had another attack when arguing with his brother." The impact of this case is powerful. Here is a man who had cataplexy on pleasant, as well as unpleasant, emotion; yet his first three attacks were evoked by aggressive impulses.

The Jaw in Cataplexy.—Many patients stress the paralysis of the jaw. Thus, in Drake's [13] Case 2 the patient described his attacks in these words: "First my jaw opens wide and then my legs get weak, and then, bam, I drop to the ground in a heap." In Bostock's [18] Case 2 the patient "could control [his attacks] by holding his jaw." This importance of the jaw may be related to the fact that the jaw is the most primitive organ of aggression. The infant can bite before he can strike or scratch.

CATAPLEXY ON LAUGHING

We have progressed from the conscious and guilt-provoking hostility of anger to the equally conscious, but permissible, aggression of hunting and fishing, and thence to the unconscious aggression of play. Continuing in the same direction, we arrive at the problem of laughter. The sequence of events discussed thus far, namely,

the upsurge of an aggressive impulse followed by cataplexy, is clearly a matter of conditioned inhibition. In contrast, the mechanism of cataplexy on laughter is a baffling mystery.

Many people have pointed out that cataplexy is an exaggeration of a normal phenomenon, expressed when we say we are "weak with laughter." This may be true, but it does not explain anything.

To my statement that cataplexy on laughter is a mystery there is one exception. Some laughter is based on hostility. It is no accident that in a country where cruelty and brutality are given free rein the leading magazine of humor is named *"Krokodil."* When laughter that is hostile is followed by cataplexy, we do see conditioned inhibition at work. An example is in Zehrer's [26] Case 2: The patient was stricken when laughing at a deaf-mute trying to express himself. Conditioned inhibition was associated here with shame. Another example is Barker's [21] Case 1. The patient, who often had cataplexy when cross with her children, had an attack on Christmas Eve, when her husband came home drunk and she was "roaring" at his comical behavior; but she was also angy, for, as she said, "It was a hell of a thing to do . . . Of all the times to get drunk . . . The kids were expecting him to play Santa Claus."

In the two examples just given, laughter was associated with hostility that was conscious. Sometimes it is associated with unpleasant emotions that are unconscious. This probably happened in an incident reported by Coodley's [6] patient, who had his first attack of cataplexy in the following circumstances: He was out on the firing range, and, among others, the colonel was there. The colonel was beloved by all and was known as "Sunny Jim."

> The patient had forgotten to carry out some minor detail and when the colonel discovered it, he ran after the patient in a kidding manner as if to grab him. The patient had run only a very short distance when suddenly his knees buckled [and] he fell to the ground.

The case history shows that the patient had feared his father, who had threatened him with castration if he ever caught him "taking advantage" of a girl. When the colonel chased him, though only in mock anger, the mock fright with which the patient responded must have concealed some unconscious fear and hostility from the father-situation, and so there was conditioned inhibition.

But why laughter that is not hostile should evoke cataplexy is a mystery.

SUMMARY

Impulses of an aggressive nature, when associated with guilt, may evoke cataplexy. The aggression may be real and overt, as when a man raises his hand against his child. It may be real, but only implicit, as when he has a hostile wish or thought. It may be associated with guilt, even though it is permissible, as when he is about to fire at game or haul in a fish. It may take the naked form it does in some sports, as in boxing. Finally, it may be symbolic, as in a sport like tennis. When aggression is justified and is therefore not provocative of guilt, cataplexy is not likely to occur. Thus, a narcoleptic person was able to punish a man who had made fun of his infirmity, and there was no paralysis to stay his hand.

350 Central Park West (25).

26. Zehrer, H.: Zur Klinik der Narkolepsie, Allg. Ztschr. Psychiat. **92**:263-269 (Dec. 20) 1929.

RETRACTION NYSTAGMUS AND RETRACTION OF EYELIDS DUE TO ARTERIOVENOUS ANEURYSM OF MIDBRAIN

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PARINAUD'S syndrome is regarded as the result of a supranuclear lesion in the region of the midbrain. In addition to the disturbances of conjugate upward movements, pupillary abnormalities are often found in association, the lesion then being assumed to be in the vicinity of the afferent pupillomotor pathways.

In rare instances Parinaud's syndrome is associated with retraction nystagmus, and still more uncommonly these two disturbances are accompanied by retraction of the lids.

The combination of Parinaud's syndrome and retraction nystagmus is not unknown, Walsh,[1] citing Bárány in this connection. Kestenbaum[2] described a syndrome of the Sylvian aqueduct which, when complete, consists of the following signs: paralysis of vertical upward gaze (collicular sign), tonic convergence spasms occurring on attempted upward gaze, attacks of clonic convergence, movements, retraction nystagmus, nystagmus on vertical gaze upward or downward, pupillary disturbances, and paresis of one or more extrinsic eyemuscles.

Retraction nystagmus, first described by Elschnig, is an involuntary rhythmic retraction of the eyeballs during attempted voluntary eye movements in any direction. By Walsh and Kestenbaum retraction nystagmus was considered essentially the same as rhythmical convergence spasms. Spiegel and Sommer[3] explained the syndrome as being due to pressure upon the posterior longitudinal fasciculi and preponderance of tonus of the rectus muscles, which pull the eyeballs into the orbit. Bielschowsky[4] implicated the cumulative impulses originating through compression of the entire nuclear region.

As etiologic factors in retraction nystagmus have been described tumors in the vicinity of the aqueduct (Elschnig), tectal tumors (Bárány), cysts (Cysticercus,

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1. Walsh, F. B.: Clinical Neuro-Ophthalmology, Baltimore, Williams & Wilkins Company, 1947.

2. Kestenbaum, A.: Clinical Methods of Neuro-Ophthalmologic Examination, New York, Grune & Stratton, Inc., 1946.

3. Spiegel, E. A., and Sommer, I.: Neurology of the Eye, Ear, Nose and Throat, New York, Grune & Stratton, Inc., 1944.

4. Bielschowsky, A.: In Handbuch der Neurologie, Edited by O. Bumke and O. Foerster, Berlin, J. Springer, Inc., 1936. Vol. 4, p. 204.

Elschnig), encephalitis of the cerebral peduncles, and syphilis or progressive degenerative disease of the ocular nuclei, and these authors are cited by Bielschowsky.[4]

We are aware of recent publications on retraction nystagmus (Wilke,[5] Smith and Riesenman,[6] Heim,[7] Ody and Metzger,[8] Tronconi,[9]) but these papers have been unavailable to us.

Retraction of the lids combined with Parinaud's syndrome is recognized, although we fully agree with Collier [10] that little attention has been paid to it, nor were we able to find a reference in the literature to the combination of retraction nystagmus and retraction of the lids in the same patient. "It is by no means a rare event," said Collier of retraction of the lids, "while ptosis has been one of the sign-manuals of quadrigeminal and sympathetic lesions since the days of Nothnagel." He cited Gowers' description, "and in total palsy without ptosis a staring look results." He also mentioned a case in which a total external ophthalmoplegia of long standing, presumably due to a vascular lesion, was associated from the time of its commencement with intense and unvarying retraction of the eyelids.

Collier presented three case reports, one with necropsy findings, of patients who suffered a vascular accident and then presented retraction of the lids. Two patients had retraction of one lid and drooping of the other. He concluded that "the lesion responsible for the tucked lids and large pupils is situated farther forwards than is the lesion productive of ptosis and small pupils." He postulated the lesion to be not farther back than the posterior limit of the posterior commissure. From his last two cases he concluded that the mechanisms for retraction and ptosis are strictly unilateral, since the two conditions may coexist.

Retraction of the lids, as described above, should not be confused with the so-called pseudo-Graefe sign, since it is constant and the pseudo-Graefe sign, on the other hand, is visible only during attempted gaze downward and is a so-called synkinetic movement, or comovement (Kestenbaum).

As mentioned above, Collier considered a vascular lesion to be the cause of the long-standing retraction of the lids in one of his cases. In a recent study, Chavany and Auvert [11] demonstrated by arteriography in one of three cases of retraction of the lids accompanied by Parinaud's syndrome the presence of a small congenital aneurysm of the posterior cerebral artery. In the two other cases a space-occupying lesion was incriminated. Their interpretation of the retraction as hypertonia of Mueller's muscle is questionable, considering the very poor development in man of this muscle and the absence of exophthalmus in their cases, as in ours. If we accept the explanation of lid retraction on the basis of impulses conveyed by sympathetic fibers, we would suggest that the tonus of the superior tarsal muscle plays the more important role, while it is responsible for the width of the palpebral fissure. It is beyond the scope of the present paper to discuss the possible explanations—whether impulses from the lateral oculomotor nuclei or sympathetic impulses play the more important role in the mechanism of retraction of the lids.

5. Wilke, G.: Arch. Psychiat. **113**:388, 1941.
6. Smith, H. C., and Riesenman, F. R.: Arch. Ophth. **33**:13, 1945.
7. Heim, M.: Ophthalmologica **110**:15, 1945.
8. Ody, F., and Metzger, O.: Confinia neurol. **8**:222, 1947.
9. Tronconi, V.: Riv. oto-neuro-oftal. **24**:195, 1949.
10. Collier, J.: Brain **50**:488, 1927.
11. Chavany, J. A., and Auvert, B.: Presse méd. **59**:346, 1951.

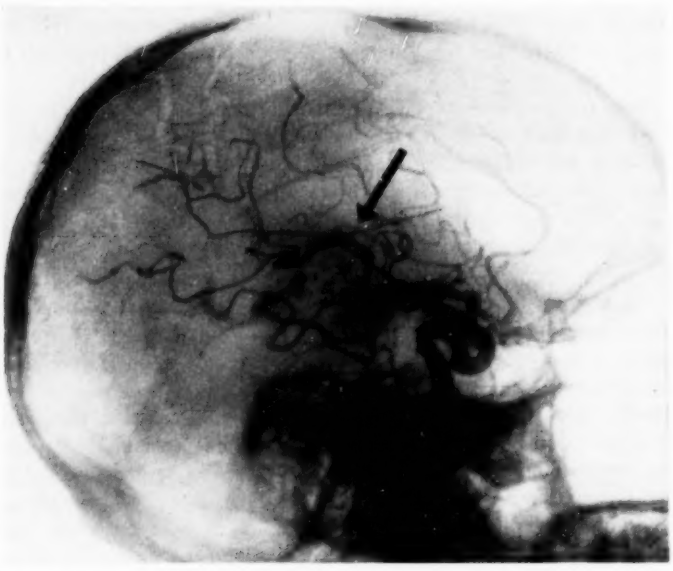

Fig. 1.—Left arteriogram, showing vascular malformation (indicated by the arrow). The draining great cerebral vein of Galen and the sinus rectus (straight sinus) have become apparent.

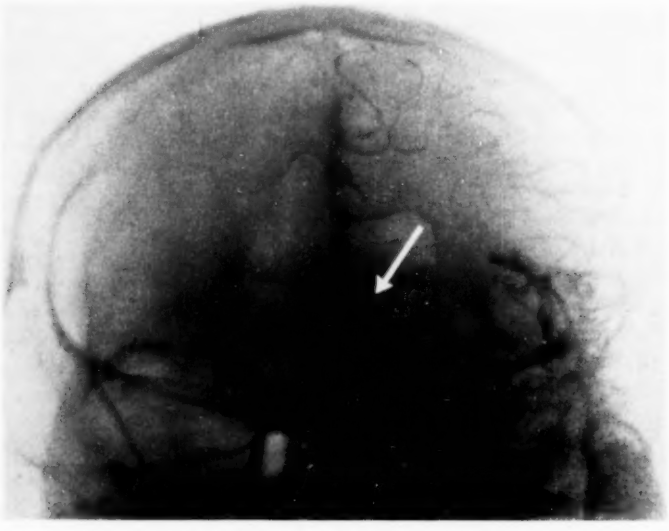

Fig. 2.—Posteroanterior arteriogram.

REPORT OF A CASE

E. J., aged 36, was hospitalized in May-June, 1950; March-April, 1951, and August, 1951.

Three weeks before his first admission to this department the patient suddenly collapsed on the street and was admitted to the Hadassah Hospital, Tel-Aviv, where he was unconscious for two days. Several days later he was able to state that before his attack he suffered from headaches and vertigo. He presented motor weakness and numbness of his right arm and leg and slight motor aphasia. He was transferred then to this department.

The patient had been healthy, and the family history was noncontributory.

Our first neurological examination disclosed paresis of the right side of the face, and signs of motor aphasia (the patient was right-handed). The blood pressure was 130/90. The general clinical examination and examination of blood and urine revealed nothing abnormal. Spinal puncture yielded hemorrhagic fluid. The Wassermann and Kahn reactions of the blood and the spinal fluid were negative. Ophthalmological examination and roentgenograms of the skull revealed no abnormality. Percutaneous arteriography (left side) revealed an arteriovenous aneurysm, located to the left of the midline in the region of the midbrain (Figs. 1 and 2). The feeding arteries came partly from the posterior cerebral artery and partly from the Sylvian vessels; the draining veins were the great cerebral vein (of Galen) and the sinus

Fig. 3.—*A*, patient during his second admission, showing retraction of the eyelids. *B*, the patient when he was 18 years old; the staring look was produced by retraction of the eyelids.

rectus; the anterior cerebral artery was tortuous. This aneurysm had eventually led to a subarachnoidal hemorrhage.

Pneumoencephalography showed no gross malformations of the ventricular system, so that presumably the possibility of a highly vascularized brain tumor was ruled out.

The patient was discharged one month later, under medical supervision. He was much improved but still complained of occasional headaches; in the following months he was able to perform his regular duties as a town clerk.

In March, 1951, while in his office, he suddenly complained of headaches, vertigo, and nausea and noticed paraesthesias of his right arm and leg. He did not remember what happened afterward, although he was not unconscious. He vomited heavily and was admitted again to this department.

On admission he was somnolent but not unconscious. The blood pressure was 115/80. There was no stiffness of the neck. Neurological examination revealed Parinaud's syndrome, absence of pupillary reflexes, spastic hemiparesis of the right side, including the face, and moderate motor aphasia. The spinal fluid was hemorrhagic, and the pressure was increased. The bleeding time was 2 minutes; coagulation time, 6½ minutes; prothrombin time, 65%, and thrombocyte count, 225,000 per cubic millimeter.

Ophthalmological Examination.—On his attempting to look straight ahead, the gaze of the patient was directed slightly downward; on the contrary, he bent his head backward when

trying to fix objects above the horizontal; when half-reclining in bed, he looked constantly at his feet. The upper eyelids were lifted and retracted, so that a strip of sclera was visible above the cornea—retraction of the lids (Fig. 3*A*).

Motility of the Eyes: 1. Command movements were executed normally to the right, left, and downward. Symmetrical first-degree nystagmus occurred to the right and to the left. Upward movements performed on command were not elicitable, both eyeballs remaining in the resting position.

2. Optically elicited movements were performed in essentially the same way as those described in 1.

3. Following movements to the right, left, and downward were normal. In an upward direction the eyes followed only 2 to 3 mm. from the original position.

4. Quick passive downward rotation resulted in a counterrotation of the eyes upward (Bielschowsky's phenomenon in paralysis of conjugate eye movements), almost of normal excursion, although the eyes immediately returned to the original position. This reflex movement was a compensatory function of vestibular origin.

Eye Muscles: There was complete convergence paresis.

Synkinetic Movements: On all voluntary attempts at eye movements, especially those of convergence and upward gaze, rhythmical jerking retraction movements of the eyes, with an incursion of 3 mm., were seen. This retraction nystagmus was not seen with the eyes at rest. When attempted lid closure was prevented by the examiner, both eyes moved upward in the same degree, constituting a normal Bell phenomenon.

Pupils: The pupils were slightly dilated (5 mm.) and irregular, and the reactions to light and in convergence were absent.

Visual Fields: The visual fields were full.

Ophthalmoscopical Examination: The media were normal, with overfilling of the fundal veins. The patient did not present any vascular abnormalities of the retina or cutaneous nevi with mental changes, such as were described by Wyburn-Mason.[12]

In this case arteriography and pneumoencephalography permitted us to make a diagnosis of the localization, as well as the nature, of the lesion with confirmation later by the neuro-ophthalmological signs and symptoms.

We decided against direct exploration, having in mind the localization and the nature of the lesion, and, after some hesitation, against ligature of the left internal carotid artery, since we feared accentuation of the existing right hemiplegia and the motor aphasia. X-ray therapy alone was given.

Three weeks after the hemorrhage, and before the x-ray therapy was started, the retraction nystagmus had disappeared. At a follow-up examination in August, 1951, the man was still disabled by his severe hemiparesis. He still presented retraction of the lids and Parinaud's syndrome.

[In March, 1952, a third hemorrhage occurred. We then decided to perform a ligature of the left common carotid artery.]

GENERAL COMMENT

This patient, then, presented a history of two subarachnoidal hemorrhages in a period of 1½ years, the second of which produced a curious mesencephalic syndrome, consisting of three rare clinical signs and symptoms. This syndrome has probably been seen in part by most observers but, so far as we know, has not previously been described in such complete form. The etiologic factor in the syndrome in our case was also unusual, being neither a tumor nor a cyst, as described in Elschnig's cases, but a paramesial arteriovenous aneurysm on the left side of the midbrain, demonstrated arteriographically.

Although Collier postulated a vascular lesion in one of his cases, he had not the means to demonstrate conclusively that a malformation was associated with long-

12. Wyburn-Mason, R.: Brain **66**:163, 1943.

standing lid retraction. Chavany and Auvert's first patient had an aneurysm but did not present retraction nystagmus.

The presence of Bell's and Bielschowsky's phenomena in our patient, with the inability to raise his eyes voluntarily, indicates that the lesion was supranuclear. In accordance with Collier's localizing suggestions, we propose that the region of the posterior commissure was involved in this case.

Kestenbaum described four types of paralysis of vertical gaze. According to his classification, our case belongs to Type 3, the Oppenheim type (optical elicited movements and schematic movements involved; vestibular and following movements free, or almost free). Since the retraction of the lids in our case gives a hint of localization, we can perhaps answer Kestenbaum's dictum: "We have no knowledge about the size of the lesion in Types 3 and 4."

It is interesting that some weeks after the last hemorrhage the retraction nystagmus disappeared, while Parinaud's syndrome and retraction of the lids were still present. This is contrary to the observation of Chavany and Auvert that retraction of the lids disappeared rather rapidly while Parinaud's syndrome persisted. These authors assumed retraction of the lids to be a more labile symptom, dependent on the increased intracranial pressure. Our patient's relatives told us, however, that he had had a "staring look" from childhood, as seen in a photograph taken when he was 18 years old (Fig. 3 *B*).

We assume that his vascular malformation was congenital, causing permanent involvement of certain structures in the mesencephalon, followed by lasting retraction of the eyelids. His hemorrhage was partly in the brain tissue, partly leaking into the subarachnoidal space. Destruction of brain tissue caused a permanent Parinaud syndrome, while temporary local edema might account for the retraction nystagmus, which lasted only for a few days, although the last problem needs further elucidation.

SUMMARY

An account is given of some neuro-ophthalmological signs and symptoms associated with lesions of the midbrain.

A case is described in which a combination of retraction nystagmus, retraction of the lids, and Parinaud's syndrome followed the last of two subarachnoidal hemorrhages in a patient who was found, by arteriography, to have a vascular malformation in the midbrain.

So far as is known, this case is unique.

Possible mechanisms for production of the syndrome are discussed, and the scanty literature is reviewed.

Beilinson Hospital.

Dr. R. Stein assisted in the neuro-ophthalmological study, and Dr. H. Salinger, in the x-ray examinations.

BILATERAL ENCAPSULATED SUBDURAL EFFUSION COMPLICATING BACTERIAL MENINGITIS IN INFANCY

Report of a Case with Review of Literature

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RECENT reports in the pediatric literature have emphasized the occurrence of subdural effusions as a complication of purulent meningitis. This has become apparent only since the advent of therapy with antibiotics. The majority have occurred in infections with Hemophilus influenzae and Diplococcus pneumoniae, with only four cases reported due to Neisseria meningitidis. As the number of papers on this subject increases, it becomes obvious that effusions may occur in purulent meningitis caused by a variety of organisms and that no specificity in this regard may be ascribed to any one in particular.

It is the purpose of this paper to present the fifth case of meningitis caused by N. meningitidis in an infant complicated by the presence of bilateral encysted subdural effusions. The literature covering all the reported cases of subdural effusion occurring in the course of recovery from bacterial meningitis is reviewed. The clinical aspects are discussed, as well as the pathology, therapy, and possible sequelae.

REPORT OF CASE

A 10-month-old boy was admitted to the Gouverneur Hospital with fever and persistent vomiting. He had been well until two days prior to admission, when he became febrile. At that time the diagnosis of tonsillitis was made, and he was treated with intramuscular injections of penicillin. The fever continued, and the child did not seem to improve. He became somnolent and irritable, and projectile vomiting occurred three times on the day prior to admission.

The child had been delivered normally and spontaneously at term, weighing 6½ lb. (2,948 gm.). He sat alone at 7 months and had his first tooth at 6 months of age. He did not stand or talk. There was no history of a childhood exanthem.

On admission, he was noted to be acutely ill. He was unusually well developed and well nourished. His temperature was 103 F. His skin was slightly pale, warm, and dry, with no evidence of a rash. Although lethargic, he was irritable when aroused. The circumference of his head was 49.2 cm., which, although large, was not disproportionate to his general body habitus. The anterior fontanelle was tense but not bulging. The conjunctival membranes were not injected, and there were no petechiae. The tonsils were enlarged and cryptic. There was no evidence of ear disease. Respirations were 48 per minute. The heart rate was 168 a minute; the rhythm was regular, and the sounds were of good quality. The remainder of the physical examination was noncontributory.

From the Department of Surgery, Division of Neurological Surgery, and the Department of Pediatrics, Gouverneur Hospital.

Neurological examination revealed nuchal rigidity, with positive Kernig and Brudzinski signs. The knee jerk was of normal intensity on both sides. There was no gross evidence of weakness or of sensory abnormalities. The pupils were round, regular, and equal and reacted well to light. Funduscopic examination disclosed no abnormalities.

Blood studies disclosed 9.0 gm. of hemoglobin per 100 cc., with 4,310,000 red cells and 20,700 white cells, of which 70% were polymorphonuclear leucocytes and 30% were lymphocytes.

Spinal puncture revealed cloudy fluid under increased pressure. The fluid contained 1,192 white cells per cubic millimeter. The Gram stain revealed Gram-negative diplococci. The sugar content was 40 mg.; the protein, 150 mg., and the chlorides, 710 mg., per 100 cc. Culture revealed N. meningitidis Types I and III, which were later found to be sensitive to penicillin, aureomycin, chloramphenicol (chloromycetin®), and oxytetracycline ("terramycin").

The child was given 500 mg. of chloramphenicol, and this was repeated in 250 mg. doses every six hours by intramuscular injection. He also received syrup of sulfisoxazole (gantrisin®), 1 tsp. every four hours, and 500,000 units of aqueous penicillin G, initially intramuscularly, and 200,000 units every two hours thereafter. One cubic centimeter of lipo-adrenal cortex (a

Fig. 1.—Roentgenogram of the skull taken after replacement of 10 cc. of subdural fluid with air. The subdural sac over the convexity of the brain is defined in part, as well as its extension medially along the longitudinal fissure. The superior cerebral veins entering the sagittal sinus are well demonstrated (arrow).

preparation of steroid hormones of the adrenal cortex dissolved in vegetable oil) was given daily.

His temperature fell to normal in eight hours, but on the third hospital day it spiked to 103.2 F. and remained between 101 and 102 F. until the 10th hospital day, when it again rose to 103.8 F. Lumbar puncture on the ninth day disclosed 46 white blood cells per cubic millimeter, of which 26 were polymorphonuclear leucocytes and the remainder lymphocytes. Protein measured 32 mg.; sugar, 74 mg., and chlorides, 710 mg., per 100 cc. No organisms were seen in smears. On the 12th day a bilateral subdural tap was performed because of the persistently elevated temperature in the face of adequate antibiotic therapy and a sterile spinal fluid. Ten cubic centimeters of cloudy, xanthochromic fluid was obtained from the right subdural space.

but no fluid from the left. On the 14th day, the right side yielded 3 cc., and the left, 22 cc. of turbid, golden-yellow fluid. On the 16th day 5 cc. of similar fluid was removed from the right side and none from the left. On the 18th day 20 cc. was removed from the right space and 5 cc. from the left. The protein content of the subdural fluid varied from 450 to 640 mg. per 100 cc., and the sugar was 95 mg. per 100 cc. on one occasion. The red blood cells, both fresh and crenated, varied from 2,500 per cubic millimeter to as high on one occasion, as 220,000 per cubic millimeter. White cells were present in varying amounts. On one occasion there were

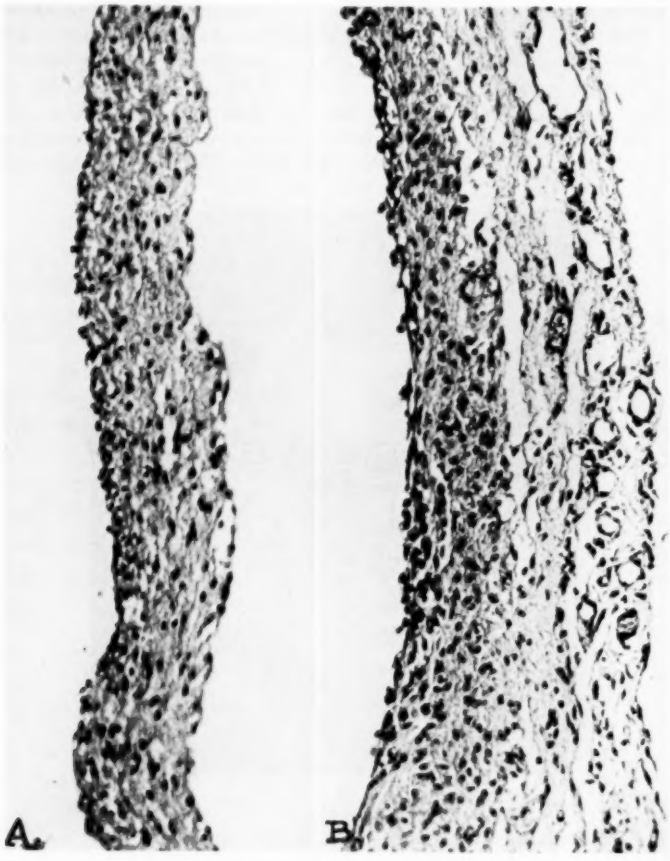


Fig. 2.—*A*, section of membranes removed at the first operation, on the 25th hospital day, showing essentially gramulation tissue; *B*, section of membrane removed at second operation, 60 days after admission to the hospital, showing the well-formed fibrous tissue layer and the prominent newly formed vessels in the zone of granulation. × 260; hematoxylin-eosin stain.

110 polymorphonuclear leucocytes and 320 lymphocytes; on a second, 25 lymphocytes, and on a third, 8 lymphocytes, per cubic millimeter. At no time were organisms identified on smear or culture.

On the 23d hospital day an electroencephalogram was recorded. This showed 4- to 6-per-second waves of medium to moderately high voltage in all leads, with occasional slow potentials and some scattered 7- to 9-per-second waves. Low-voltage fast, 20- to 25-per-second waves were

superimposed upon the other wave forms. No significant asymmetries were noted, and the record was regarded as normal for a child of the patient's age.

On the 25th hospital day a right frontotemporoparietal craniotomy was performed, with the use of general endotracheal anesthesia. At first, a temporal burr hole was made after the technique described by Ingraham and Matson,[1] and a very thin grayish membrane adherent to the under surface of the dura was identified. A large bone flap, approximately 10 cm. in its greatest diameter and hinged on the temporal muscle, was then turned. The dura was reflected over the exposed area, disclosing a sac composed of thin but well-formed membranes, containing yellow-brown fluid. The membranes were stripped, without difficulty, from the under surface of the dura and from the surface of the arachnoid membrane over as wide an area as possible. The dura was closed tightly and the bone flap replaced. The wound healed without incident.

On the 32d hospital day 6 cc. of xanthochromic fluid was obtained from the left subdural space; on the 44th day 10 cc. was obtained. On the 55th day, 10 cc. of fluid was replaced with an equal volume of air. Roentgenograms taken with the head in a variety of positions outlined the extent of the encysted fluid and gas, indicating that, in addition to the expected location of the effusion over the convexity of the brain, there was a considerable extension along the longitudinal fissure medial to the falx cerebri (Fig. 1). The air was not visualized in roentgenograms taken five days later.

A second craniotomy was performed on the 60th hospital day. At operation the extension of the membranous sac into the longitudinal fissure was confirmed. It was impossible, however, to remove the membranes in this location without injuring the superior cerebral veins, which bridged the subdural space to enter the superior sagittal sinus.

Microscopic examination of the membranes removed at operation disclosed granulation tissue, with interspersed connective tissue fibers forming a well-defined band in the latter specimen. No evidence of acute inflammation was seen. Only a rare pigment-laden phagocyte and eosinophile was observed (Fig. 2).

The postoperative course was complicated by a wound infection with Micrococcus pyogenes var. aureus and Aerobacter aerogenes. After the bone flap was removed, wound healing occurred without difficulty. The patient was discharged 126 days after admission, at which time the circumference of his head measured 50 cm. He had developed normally during this period, had learned to stand, and showed no evidence of retardation or any sign of a residual cerebral complication of his infection.

COMMENT

The introduction of specific antisera, the sulfonamides, penicillin, and the newer antibiotics has resulted in a remarkable fall in mortality and morbidity in acute bacterial meningitis. However, sufficient evidence of impaired cerebral function has persisted. This has been well documented in infancy and in early childhood by Waring and Weinstein[2] in pneumococcic meningitis and by Crook, Clanton, and Hodes[3] in H. influenzae meningitis. Included among the more serious residua are optic nerve atrophy with blindness, deafness, strabismus, hydrocephalus, spastic monoplegias and hemiplegias, hemiparesis, and signs of intellectual deficiency. For children under one year of age the complete recovery rate was appreciably lower than that for older age categories. This has been related to such factors as the poorer resistance to infections in this group and to the frequency of a delay in the diagnosis of meningitis in an infant, even under the best

1. Ingraham, F. D., and Matson, D. D.: Subdural Hematoma in Infancy, J. Pediat. **24**:1 (Jan.) 1944.

2. Waring, G. W., Jr., and Weinstein, L.: Treatment of Pneumococcal Meningitis, Am. J. Med. **5**:402 (Sept.) 1948.

3. Crook, W. G.; Clanton, B. R., and Hodes, H. L.: Hemophilus Influenzae Meningitis: Observations on the Treatment of 110 Cases, Pediatrics **4**:643 (Nov.) 1949.

of circumstances. In pneumococcic meningitis, serious prolonged or permanent neurological complications were described in about 20% of the penicillin-treated patients.[2] In the follow-up study of 110 infants and children with Hemophilus influenzae, severe brain injury was found in 17%. Little, if any, improvement occurred in those patients who manifested signs of residual cerebral damage at discharge. Of the group below one year of age, 50% recovered completely, as compared with 75% of the older group.[3]

In a recent review by Ross [4] of the neurological sequelae in patients with meningococcic meningitis receiving serum, sulfonamides, and sulfonamide-penicillin therapy, 51 were followed by means of physical and neurological examinations. On 32 patients electroencephalographic and psychometric studies were also performed. Nineteen, or 59%, of the latter group were shown to have residual brain damage. Of the serum-treated patients, seven (78%) had a total of 10 defects; of the sulfonamide-treated group, nine (56%) had a total of 12 defects, and of the group given the combined sulfonamide-penicillin therapy, three (43%) had 1 defect each. The complications occurring with combined therapy were transient. Those occurring with the earlier methods of treatment were often of a permanent and disabling nature, such as panophthalmitis, deafness, and cerebral vascular thrombosis. Ten (32%) of the patients evaluated psychometrically exhibited evidence of cerebral dysfunction. It was believed the personality and psychiatric defects observed were the result of meningococcic encephalopathy.

A review of a large number of reported cases of meningococcic meningitis disclosed no mention of subdural effusions complicating the infection.[5] In two cases, both of adults, acute subdural hematomas were discovered at autopsy to be contributory causes of death six and seven days, respectively, after the onset of symptoms of meningitis.[6]

The first published report of subdural effusions complicating the course of influenza meningitis was that of McKay, Morissette, Ingraham, and Matson.[7]

4. Ross, A. T.: Meningococcic Meningitis: Incidence of Residua Following Serum, Sulfonamide, and Sulfonamide-Penicillin Therapy, A. M. A. Arch. Neurol. & Psychiat. **67**:89 (Jan.) 1952.

5. (*a*) Denehy, W. J.: Meningitis, Brit. M. J. **2**:684 (Nov. 18) 1916. (*b*) McLean, S., and Caffey, J. P.: Sporadic Meningococcic Meningitis: Sequelae Following Specific Serum Therapy in Infancy and Early Childhood, J. A. M. A. **87**:91 (July 10) 1926. (*c*) Slesinger, H. A.: Complications and Sequelae of Meningococcic Meningitis During Infancy and Childhood, Pennsylvania M. J. **36**:327 (Feb.) 1933. (*d*) Ballard, S. I., and Miller, H. G.: Sequelæ of Cerebrospinal Meningitis: An Analysis of 60 Cases, Lancet **2**:273 (Sept. 1) 1945. (*e*) Hoyne, A. L., and Brown, R. H.: Seven Hundred and Twenty-Seven Meningococcic Cases: An Analysis, Ann. Int. Med. **28**:248 (Feb.) 1948. (*f*) Kaufman, B.; Levy, H.; Zaleznak, B. D., and Litvak, A. M.: Statistical Analysis of 242 Cases of Meningococcus Meningitis, J. Pediat. **38**:705 (June) 1951.

6. Banks, H. S., and McCartney, J. E.: Meningococcal Encephalitis, Lancet **1**:219 (Feb. 21) 1942. Nelson, J.; Clyne, R. M., and Sharnoff, J. G.: Bilateral Subdural Hematoma—an Unusual Complication of Meningococcus Meningitis, Ann. Int. Med. **25**:862 (Nov.) 1946.

7. McKay, R. J., Jr.; Morissette, R. A.; Ingraham, F. D., and Matson, D. D.: Collections of Subdural Fluid Complicating Meningitis Due to Haemophilus Influenzae (Type B): Preliminary Report, New England J. Med. **242**:20 (Jan. 5) 1950.

This was followed by reports of this complication in other types of meningitis by Smith, Dormont, and Prather,[8] Ried,[9] Arnold,[10] and Steinberg and Murphy.[11] The accompanying table lists the organisms identified with the meningitic infection and the number of subdural effusions reported in each category.

Of the total of 39 cases now reported, the effusion has been recorded as complicating meningococcic meningitis in only 4.

Positive cultures of the subdural fluid have not been obtained in any case of meningococcic meningitis. However, of the six positive cultures reported, H. influenzae was identified in four, D. pneumoniae in 1, and the paracolon bacillus in one.[12] The finding of positive cultures is the most significant factor in determining the cause of the effusions discussed. Bilateral effusion was present in the majority of patients. Membranes were found at operation in a total of 11 patients; these were bilateral in 4. Meningitis was caused by H. influenzae in eight of these patients and by N. meningitidis in three.

In 34 of the total number of cases of subdural effusion recorded the infants were under one year of age. In four the patients were between 1 and 2 years of

Number of Cases of Subdural Effusion Reported for Each Type of Organism Isolated on Spinal Fluid Culture

Organism	McKay and Others [7]	Smith and Others [8]	Ried [9]	Arnold [10]	Steinberg and Murphy [11]	Present Report	Total No. of Cases
H. influenzae	9	9	1	1	..	..	20
D. pneumoniae	..	8	..	3	..	..	11
N. meningitidis	..	1	2	..	1	1	5
Ps. aeruginosa	..	1	..	..	..	..	1
Paracolon bacillus	..	1	..	..	..	..	1
Hemolytic Streptococcus*	..	..	..	..	..	1*	1
Total cases	9	20	3	4	1	2	39

* This case, that of a 14-month-old girl with bilateral subdural effusion, was followed by one of us (J. A. E.) at the St. John's Episcopal Hospital, Brooklyn, and will be the subject of a separate report from the Department of Pediatrics.

age, and in one the child was 2½ years of age, this being the oldest patient reported with this complication. In none of the recent reports, including those with postmortem studies, has any mention been made of subdural effusions occurring in older patients with meningitis either prior to or following the introduction of antibiotic therapy.[13] It remains to be proved, as Smith and her co-workers suggested, that such effusions are limited to infants.

The rapid growth of the infant brain, doubling in the first three months of life and doubling again in the next six months,[1] may be related to the appearance

8. Smith, M. H. D.: Dormont, R. E., and Prather, G. W.: Subdural Effusions Complicating Bacterial Meningitis, Pediatrics **7**:34 (Jan.) 1951.

9. Ried, H. L.: Subdural Effusions in Pyogenic Meningitis, Clin. Proc. Child. Hosp. **7**:182 (June) 1951.

10. Arnold, G. G.: Purulent and Serous Subdural Effusions in the Course of Purulent Meningitis, J. Pediat. **39**:191 (Aug.) 1951.

11. Steinberg, S. H., and Murphy, J. P.: Subdural Hygroma Complicating Meningococcic Meningitis, J. Neurosurg. **8**:671 (Nov.) 1951.

12. McKay and others.[7] Smith and others.[8] Arnold.[10]

13. Waring and Weinstein.[2] Crook, Clanton, and Hodes.[3] Ross.[4] Denehy.[5a] Ballard and Miller.[5d] Hoyne and Brown.[5e] Kaufman and others.[5f] Banks and McCartney.[6]

of symptoms of cerebral dysfunction early in the course of the effusion. For the same reason, it is of the utmost importance to remove the membranes in these patients once they have formed. If allowed to remain, the dense fibrous envelope adherent to the pia-arachnoid restricts the normal growth of the brain and interferes with the blood supply of the underlying cortex.[1] When repeated taps of the subdural space give positive results, temporal burr holes must be made in order to determine the presence of membranes. Since these membranes are formed after a period of 2 to 3 weeks (the earliest being found in the present group after 18 days), repeated subdural taps early in the course of the illness may prevent their formation if fluid accumulations are successfully and permanently removed. In the present case, at the first operation, 25 days after admission, the membrane was of gossamer thinness and could easily have been overlooked had we not been alerted to its possible existence. At the second procedure, 60 days after admission, it was thick, well formed, and impossible to overlook.

The indications for tapping the subdural space in the course of bacterial meningitis have been well established. The persistence of fever despite evidence of an adequate bacteriologic response to effective doses of antibiotics after 24 to 48 hours is of the utmost significance. In addition, one must include focal neurological disturbances, seizures, bulging fontanelle, rapidly enlarging head, impaired state of consciousness, and persistence of poor feeding habits, with vomiting and loss of weight.

The constant high protein content of the fluid removed from the subdural space indicates that the subdural effusions are exudates related to the meningeal inflammation. The fluid differs from that of acute traumatic subdural hygroma, in which cerebrospinal fluid enters the subdural space through a tear in the arachnoid membrane. The protein content of the fluid in this condition is low unless there is an admixture of blood, resulting from injury to the underlying brain.[14] The cases of chronic subdural effusion following mastoid and middle-ear infection in infants described by Penfield[15] and by Dandy[16] as a type of chronic subdural hygroma are of interest in that the fluid collections are reported to have arisen as a reaction to infection.

Several characteristics are shared by chronic encapsulated subdural effusion and chronic subdural hematoma after the red blood cells and the products of cellular disintegration in the latter have been resorbed.[1] As in subdural hematomas, subdural effusions are predominantly bilateral, and the fluid possesses a high protein content. The membranes described and illustrated in the present case have the usual morphology of those found in subdural hematoma. Of significance, however, is the singular absence of pigment-laden phagocytes and eosinophiles, which are found in great numbers in the membranes of subdural hematomas

14. DaCosta, D. G., and Adson, A. W.: Subdural Hydroma, Arch. Surg. **43**:559 (Oct.) 1941.

15. Penfield, W. G.: Subdural Effusion and Internal Hydrocephalus: Study of Case with Recovery, Am. J. Dis. Child. **26**:383 (Oct.) 1923.

16. Dandy, W. E.: Surgery of the Brain: A Monograph, in Lewis' Practice of Surgery, Hagerstown, Md., W. F. Prior Company, Inc., 1945, Vol. 12.

of comparable age. The finding of positive cultures in six of the subdural effusions reviewed further establishes the condition as a distinct nosologic entity.

SUMMARY

A case is presented of meningococcic meningitis in a 10-month-old infant complicated by the presence of bilateral encapsulated subdural effusion necessitating surgical removal. This complication has become apparent only since the advent of therapy with the sulfonamides, penicillin, and the newer antibiotics and has been reported exclusively in the pediatric literature. A total of 39 cases has been accumulated from all available reports. This complication may occur in the course of bacterial meningitis caused by a variety of organisms, including at the present time H. influenzae, D. pneumoniae, N. meningitidis, Ps. aeruginosa, the paracolon bacillus, and a hemolytic Streptococcus.

The significant clnical features leading to early diagnosis are discussed. The pathogenesis of the lesion, the methods of management, and the possible sequelae of bacterial meningitis are evaluated in the light of present therapy with the antibiotics.

36 E. 38th St. (16).

116 Fulton Ave. Hempstead, N. Y.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

William Malamud, M.D., Presiding
Regular Meeting, March 20, 1952

Persistence of a Tremor Consequent upon Acquired Liver Cell Disease. Dr. Joseph M. Foley.

Clinical observations were presented in three cases which had in common the unusual feature of a persistent tremor of long duration consequent on acquired liver cell disease. The tremor was of the same character as that seen in the earlier stages of hepatic coma.

Case 1.—A man aged 50 with portal cirrhosis consequent upon prolonged chronic alcoholism had severe liver cell disease and recurrent ascites. While he was hospitalized for control of his ascites, a characteristic tremor developed and continued until his death, 123 days later. The tremor was associated with a moderate degree of intellectual deficit.

Case 2.—A man aged 51 had portal cirrhosis on the background of chronic alcoholism. During a period of acute hepatic insufficiency and portal obstruction, there developed a characteristic tremor, which persisted even after the bilirubinemia had disappeared. The tremor became more pronounced and was associated with other signs of cerebral disorder during an episode of impending hepatic coma, precipitated by infection. After having been present in varying intensity for approximately 233 days, the tremor disappeared and had not recurred at the time of the report, three months later.

Case 3.—A man aged 64 with portal cirrhosis of at least five years' duration, of nonalcoholic origin, had onset of episodes of mental confusion, dysarthria, and tremor three years prior to the time of this report. For the preceding two years the characteristic tremor had been present. It was associated with a mild degree of intellectual deterioration.

These cases provide evidence that acquired liver disease may lead to a chronic neurological disorder in which tremor is the most characteristic feature.

DISCUSSION

Dr. Leo Alexander: Dr. Foley mentioned the characteristic aspects of the tremor. Was there "wing flapping" at rest?

Dr. Paul B. Jossmann: The syndrome described, in which mental symptoms are combined with persistent tremor in chronic alcoholism, has some similarity to polioencephalitis hemorrhagica of Wernicke. May the localization of the pathological process in the cases described involve an area, as in Wernicke's disease?

Dr. James M. Foley: I do not know what part of the brain must be affected to produce this kind of tremor. I incline to the belief that the tremor is produced by a totality of lesions in the cortex, basal ganglia, thalamus, and cerebellum.

Neither clinically nor pathologically can this disorder be confused with the polioencephalitis of Wernicke. The pathological changes of hepatic coma are restricted to the astroglia; there is no involvement of blood vessels.

The tremor is not present at rest except in very severe cases, when the slightest stimulation is responsible for eliciting it, as in the case also of very severe cerebellar tremor.

Aspergillus Infections of the Central Nervous System. Dr. Subramani Iyer, Dr. Philip R. Dodge, and Dr. Raymond D. Adams.

Two cases of involvement of the central nervous system and meninges by Aspergillus were reported. In the first case, that of a man aged 23, there was a 10-month history of a progressive illness characterized early by bilateral involvement of the upper cervical roots and later by increased intracranial pressure. Necropsy revealed chronic productive, granulomatous leptomeningitis in the cervical region and posterior fossa. This had implicated nerve roots and produced obstructive hydrocephalus. Morphologically, typical hyphae were demonstrated in the centers of granulomas and abscesses, and Aspergillus fumigatus was cultured from the subarachnoidal exudate at necropsy. The presence of a chronic sinusitis suggested a possible portal of entry for the fungus.

In the second case, that of a 10-month-old infant, symptoms and signs of a diffuse disorder of the cerebral cortex evolved over six months, producing behavioral regression, seizures, and, finally, a state of decortication. Intracerebral calcifications, a finding hitherto not described with aspergillosis, were demonstrated roentgenologically. Necropsy revealed chronic destructive granulomatous meningoencephalitis. The granulomas contained typical Aspergillus, but cultures were not attempted.

The previously reported cases of cerebral aspergillosis were reviewed briefly.

Significance of Perceptual Rivalry Resulting from Parietal Lesion. Dr. D. Denny-Brown, Dr. J. S. Meyer, and Dr. S. Horenstein.

The study of a patient showing disorders in perception of two concurrent stimuli, of the discriminative aspects of sensation on the left side, and, on the left side, of person and of extrapersonal space gave evidence that all these perceptual disturbances were interrelated. The cause was assumed to be a vascular lesion, without aphasia or hemiplegia. The disorders were constant for over 11 months. The phenomenon of extinction was found to be directly related to the degree of difficulty in differentiating the properties of the extinguished stimulus when alone. Combinations of stimuli were treated as a unitary whole, within which poorly differentiated features were eliminated in rivalry with those better differentiated. The unit process was identified with attention, but the defect was in the differentiation served by the parietal cortex. Such defects in differentiation are manifest in spatial summation, which is held to be the true function of the parietal lobe. Disorder of spatial summation ("amorphosynthesis") is a unilateral physiologic disorder, with corresponding loss of stimulus value for cortical motor reactions ("ideational apraxia"). Visual, tactile, or other features can be accentuated by restriction of the lesion. Amorphosynthesis is sharply distinguished from bilateral loss of the perceptual symbolism of thought, speech, and imagery ("agnosia").

DISCUSSION

Dr. Paul B. Jossmann: The visual disturbance in this case consists of an attention hemianopsia with the typical characteristic, as evident, e. g., in the result of tests to find the center of a line of a circle. This symptom exhibits the general extinction phenomenon, together with special involvement of the visual space perception. I wonder whether the assumed lesion of the parietal lobe may involve the optic radiation or Areas 18 or 19 (Brodmann).

Dr. Henry R. Viets: Does this phenomenon ever apply to the viscera? Does it ever involve headache on one side and not on the other?

Dr. D. Denny-Brown: The most important conclusion is that all sensation has a spatial quality and that the defect in cases of parietal lobe lesions is a failure to synthesize that spatial quality. Extinction is one aspect of that failure, and at the parietal level it has the aspect of an all-or-none response in perception, which is what we call "morphosynthesis." The effect of perceptual rivalry in heightening this process is a normal one, and is not peculiar to cases of parietal lobe lesions. Of course, if the elementary sense data are defective, as with lesions of the peripheral nerve, cord, optic tract, or optic radiation amorphosynthesis will also be a feature of areas of parietal defect. We have no knowledge of its occurrence with visceral sensation.

The Stretch Reflex in Parkinsonism. Dr. D. Denny-Brown, Dr. H. Seyffarth, and Dr. R. Chambers.

Electromyographic observations showed that with progressive relaxation, with the limb supported, the rigidity and tremor of Parkinsonism could be temporarily abolished in the muscles in a given region. Such quiescence was most difficult to achieve in postencephalitic Parkinsonism, less difficult in paralysis agitans, and least so in arteriosclerotic Parkinsonism. In such a completely relaxed state there is a small range of stretch of both flexors and extensors (5 to 10 degrees) without resistance (the "free interval"). Greater stretch then elicits a reflex stretch response in the stretched muscle, which differs from spasticity in that the activated motor units cease activity and return in rotation as stretch continues. This stretch is a lengthening reaction unit by unit, instead of a sudden dropping out of many units together, as in the clasp-knife phenomenon. With more rapid stretch the units begin to cease discharge and return periodically as a group. This is tremor. There is a brisk shortening reaction. The genesis of tremor and rigidity can thus be demonstrated in one muscle. The interaction of these modified stretch reflexes in all the muscles determines the distribution of rigidity and tremor in a limb.

DISCUSSION

Dr. D. Denny-Brown: I should add that these phenomena can be observed by simple clinical inspection and palpation of the muscles, if one knows what to look for. Complete relaxation of the muscles at a joint is more easily obtained in arteriosclerotic Parkinsonism than in paralysis agitans, and less easily in postencephalitic Parkinsonism, when considerable perseverance is necessary. When at last the muscles are fully relaxed, it is apparent that a small stretch of either a flexor or an extensor will set up fresh contraction, which ceases as soon as the muscle is slackened. If the stretch is continued, the contraction continues for a long period. Stretch of a flexor at one joint activates the flexors at neighboring joints, with the same prolonged after-effect. For observation of the genesis of tremor at one joint, previous relaxation of the whole limb is required because of this interaction between different muscles.

William Malamud, M.D., *Presiding*

Regular Meeting, April 17, 1952

Prognosis and Progression of Parkinson's Disease in Patients Under Medical Treatment. Dr. Simon Markovich and Dr. Robert S. Schwab.

Parkinson's disease has no specific cure and is variably progressive. Estimations of the prognosis in a specific case of this condition is difficult and perplexing. The following study of 65 patients with Parkinson's disease who were followed by one of the authors (R. S. S.) from three to five years brings out certain guides that may be used in estimating the future of patients who have this malady.

The patients were all seen four to five times a year, were examined by means of a number of laboratory, as well as neurological, tests on each visit, and were under various types of medical treatment.

All the patients were assessed as to their personalities, and, for the purpose of this communication, were divided into two groups: patients with stable deviations (A type) and those who were vulnerable or subject to depressions, extensive worriers, chronic complainers, patients with extensive drive and ambition who were subject to extreme mood swings and would, in general parlance, be regarded as neurotic or as having difficult personalities (B type).

The disease was said to be nonprogressive when the laboratory and neurological findings and the subjective reports of the patient in the beginning and at the end of the study were essentially the same.

The following factors were found not to be related to progression: (1) presence or absence of a history of encephalitis in the past; (2) age at onset; (3) sex; (4) type of Parkinsonism, and (5) number of years between the study and the onset of the disease.

Personality type and clinical evidence of cardiovascular disease were found to be related to the disease, and the data are summarized in the accompanying Table.

DISCUSSION

DR. D. DENNY-BROWN: Dr. Schwab has tackled a difficult problem, and his conclusions would be clearer to me if I more clearly understood what he means by progression. We agree that emotional stress is deleterious to a patient with Parkinsonian tremor and rigidity. However, I should like to hear more of how Dr. Schwab estimated the progression of the essential disease in relation to worsening of emotional factors. Was the estimation of the state of the disease made from the patient's condition when his therapy was discontinued? There is a swing downward immediately after cessation of therapy; with some reassurance and encouragement however, but without further drug therapy, it is possible to obtain improvement. How did Dr. Schwab judge the actual level of the basic disease process then? It would seem to me that three days after removal of the patient from all drug treatment, when he had been taking a large quantity, would not be a good time at which to estimate the extent of the disease process.

I am disturbed to hear Dr. Schwab say that there was no difference between postencephalitic Parkinson disease and paralysis agitans, or at least between persons with a clear history of

Factors Showing Relation to Progression of Parkinson's Disease

Personality Type	Vascular Disease		No Vascular Disease		Total	
	Progression	No Progression	Progression	No Progression		
A	6	6	1	15	28	65
B	10	3	13	11	37	
	16	9	14	26		
	25		40			

encephalitis and those with no such history. In my experience the postencephalitic patients do reach a reasonable stable state.

DR. PAUL B. JOSSMANN: I also want to emphasize that progression differs in postencephalitic Parkinsonism and in idiopathic Parkinson's disease. In postencephalitic Parkinsonism, survival for 30 years and more has been observed frequently, whereas in idiopathic Parkinson's disease patients survive only for much shorter periods. The course of progression in encephalitic cases is rapid after onset, whereas in cases of Parkinson's disease it is slow after onset and more rapid later.

DR. HENRY R. VIETS: Dr. Schwab gives us a more complete understanding of Parkinsonism, particularly in regard to its course and prognosis. He deals with both the encephalitic and the degenerative type and has studied a large enough group of patients over a period of years to permit valid conclusions regarding their response to medication and the changes resulting from the stress and strain of life. Apparently, a considerable number of patients with Parkinsonism, both of the postencephalitic and of the degenerative type, do surprisingly well with a moderate amount of medication and a minimum amount of supervision. On the other hand, there is another group which do well only with a great deal of supervision. Indeed, the more effort that is put into anything for them, the better the results. This point is brought out by Dr. Schwab's study. The attention that a patient of this type needs is concerned not only with the continued adjustment of the drug levels and the variety of medications that can be offered him, but also with the adjustment to his environment.

DR. WILLIAM MALAMUD: What was the effect of progression of the disease on the personality of the B group? Was the progression of illness accompanied by accentuation in personality disturbances? In other words, what were the psychological effects of the disease, not necessarily in terms of organic effects on the brain, but in terms of the adjustment of the patient to a

progressive disease? Second, what type of psychotherapy was used? Dr. Viets suggested a form of supportive psychotherapy, which I am certain is very helpful. But was there any more intensive form of treatment? I should also like to know more about the two types included under the B personality type: the cyclic and obsessive-compulsive. Jelliffe spoke of obsessive-compulsive patterns which may develop as a result of the Parkinsonian syndrome. In Dr. Schwab's patients, were these traits present both before and after the onset of the disease, and was there an accentuation of these traits as the disease progressed?

Dr. Robert S. Schwab: The questions are fundamental. Dr. Denny-Brown wondered how we measured progression. We did not remove the patients from drug therapy. Each time the patient came into the office, he was subject to a number of tests, including measurement of tremor, rigidity, and grip; drawing circles; measurement of gait; tests for free swing of arms and legs and posture, and the usual neurological tests. In addition, we recorded data as to how he did at home when eating, dressing, etc. The disease was said to be nonprogressive when these tests showed essentially the same results at the beginning, at the end, and throughout the period of observation. Medicaments were changed from time to time. Agreement on the difference between progression and nonprogression was based on a series of integrated values adopted by both the authors of this paper. We have some information on the incidence of encephalitis in so-called postencephalitic Parkinsonism. Because in this series the same patients were seen over and over again, we sometimes uncovered the history of encephalitis at a later visit. A positive history was obtained in 65%. Paralysis agitans as usually classified when plotted as to progression did not show a significant difference from postencephalitic Parkinsonism.

The five years covered by the report was the length of time we followed the patients. Some had had Parkinson's disease much longer.

I am glad Dr. Viets has emphasized the need for frequent control and adjustment of medication.

We tried to determine whether the B personality was due to the disease, or whether it was made worse by the illness. We used the Rorschach test, personality inventory questionnaires, and other methods. Our results indicated no change in basic personality due to the disease. Some patients manifested a reactive depression when their disease began to interfere with their social, economical, and sexual activities. A number of patients referred for psychiatric treatment overreacted to their disease. Personality structure seemed to be unaltered by the presence of Parkinson's disease.

Pain Fibers in the Petrosal Nerves. Dr. William H. Sweet and Dr. James C. White.

Since the greater superficial petrosal nerve was implicated by Gardner, Stowell, and Dutlinger in certain types of faciocephalic pain, we investigated further the functions of the three petrosal nerves crossing the floor of the middle cranial fossa. The nerves were stimulated in conscious patients undergoing trigeminal rhizotomy or petrosal neurectomy. Stimulation of the external superficial petrosal nerve yielded pain in the eye, cheek, or temple in two patients. In only one of the four patients whose lesser superficial petrosal nerve was seen did the excitation of the nerve cause consistently definite pain; this was referred to the temple, forehead, cheek, or nose. Pain was evoked on stimulation of the greater superficial petrosal nerve in four of five patients with Horton's neuralgia (histamine cephalgia; petrosal neuralgia) and in five of nine other patients. The pain was referred to the ipsilateral ear, eye, or adjoining parts of the head and face. The response was probably not caused by efferent impulses setting up some event in the periphery, exciting pain fibers there, since the pain did not occur when the peripheral end of the divided greater superficial petrosal nerve was stimulated, did occur at the same voltage when the central end was stimulated, and persisted after trigeminal rhizotomy. The three patients with Horton's neuralgia whose clinical pain was reproduced by stimulation at operation were relieved by the neurectomy; the other two patients were not relieved.

DISCUSSION

Dr. Bertram Selverstone: Dr. Sweet and Dr. White may be interested in one of my recent cases of Horton's syndrome. The patient's complaints were typical, but, in addition, she had severe radiating pain along the mandible, without any suggestion of a trigger mechanism. After fruitless attempts at treatment by conservative measures, she agreed to exploration of the

middle fossa, with use of local anesthesia. Stimulation of an unusually large dural vessel in the position of the middle meningeal artery reproduced her pain, together with severe pain behind the eye. The artery, when followed medially, was found to emerge from the foramen ovale, rather than from the foramen spinosum. It was, of course, anatomically the accessory meningeal artery, but it was much larger than the small true middle meningeal artery, emerging from the foramen spinosum. Both vessels were divided; in addition, the mandibular nerve was sectioned because of the radiating pain in its distribution. At the time of this report, both types of pain have been relieved for several months. The greater superficial petrosal nerve was not disturbed. One wonders whether pulsations of the unusually large accessory meningeal artery could have been responsible for the radiating pain along the distribution of the mandibular nerve.

DR. JAMES C. WHITE: You may feel that stimulating these patients, with local anesthesia, is a cruel, brutal thing to do. Dr. Sweet and I have been interested in stimulating every nerve whose function is not thoroughly known. This can be done with very little discomfort, as the whole operation does not have to be done with local anesthesia. Our anesthetists have been supplementing the thorough infiltration with procaine, with a slight dose of thiopental sodium and inhalations of nitrous oxide and trichloroethylene (trilene®). Within 5 or 10 minutes of the time the gas has been disconnected one usually has a cooperative patient who can report what he feels as well as though he had been under local anesthesia the entire time. After testing has been completed, he can be put to sleep again. The next day he has little recollection of discomfort.

DR. WILLIAM H. SWEET: One must point out that a long period of observation is necessary before sound conclusions can be drawn; I fear that several months does not suffice with respect to many pain problems. This is especially true of patients with Horton's neuralgia, many of whom have long periods of remission from pain. For example, one of our patients said: "I don't know yet whether this operation has done any good, for I have severe pains only in the springtime anyway."

I am glad Dr. White emphasized that we are not being rough on the patients. The stimuli are of very brief duration, and we start with a signal that causes no pain at all and then increase it only until the patient just feels the pain. It enables the patient to report better, as well as keeping him more comfortable.

Effect of Electric Shock on a "Normal" Person Under Recent Stress: Experiment Elucidating the Influence of Electric Shock on the Defensive Operations of the Ego. DR. LEO ALEXANDER.

In this study, the stressful event was disregarded after electric shock—stripped of its associated connections—in the manner consistent with the defensive operation known as isolation. Neutral events that occurred before and after the stressful event were clearly remembered after the electric shock.

Clinical studies, to be reported elsewhere, indicate that the arousal or enhancing of active defensive operations appears to be the most decisive effect of electric shock treatment. It is probably for that reason that electric shock therapy is helpful in those conditions in which defensive operations are at a low ebb, ineffective or exhausted, as in depression and other severely regressive psychotic states, but that it is ineffective, in fact, disturbing, in those conditions in which defensive operations are already disturbingly alerted, constituting an obstacle to treatment and recovery, as in anxiety states.

DISCUSSION

DR. WILLIAM MALAMUD: Some time ago Dr. Allers, of Vienna, whom you may remember, reported the results of experiments on peripheral vision. He found that when his subjects were asked to describe the details of a tachistoscopic exposure of pictures they left out or distorted certain items in the peripheral field of vision. Subsequently these items appeared in the dreams of the subjects. In repeating these experiments on neurotic patients, I found that the items that were left out or distorted were related to the conflicts basic to the neuroses. Did Dr. Alexander get any dreams from his patient after his interviews following the accident?

DR. WILFRED BLOOMBERG: I wonder why Dr. Alexander chooses to interpret this repression, or disregard, as an example of Freud's concept of "isolation" rather than of his concept of "denial." Presumably, on the day the patient remembered the episode and disassociated the

affect from it, it was isolation, but until then it would better have been called denial. I wish Dr. Alexander would elaborate a little more on his concept of the effectiveness of shock in those disorders in which the defenses are weak and exhausted. I should have thought that a mute catatonic patient was not a person with a weak defense, but, rather, one whose defense was functioning so strongly that it was almost perfect. Yet we are familiar with the improvement in clinical status which electric shock brings about, at least temporarily, in patients with catatonic states. I am not entirely satisfied, in fact, somewhat disturbed by the generalization that weak defenses are helped by shock therapy and strong defenses are not.

DR. PAUL B. JOSSMANN: In regard to the defense mechanism mentioned by Dr. Alexander, it is surprising that there was no amnesia for the events immediately preceding the experimental shock treatment, which should have caused a severe emotional stress. It is questionable, therefore, whether the forgetting of the accident resulted from a true retrograde amnesia. I should like to have Dr. Alexander comment on the selective mechanism of forgetting in this unique experience.

DR. WILLIAM MALAMUD: I had a patient, a jockey who fell off a horse and sustained a concussion, with partial amnesia from the accident. He remembered the details but insisted that the accident happened to his uncle. It turned out to be an uncle whom he hated.

DR. LEO ALEXANDER: I agree that this problem is a fascinating one. I think I have answered Dr. Malamud's question. As to Dr. Bloomberg's point, I think that the mechanisms of isolation and of denial are closely related, both being strongly active in obsessive-compulsive states. Both these mechanisms are greatly activated after convulsive electric shock. Obsessive-compulsive states do poorly after convulsive electric shock because it enhances what they already have too much of.

Only the memory of the accident itself, which was really disturbing to the subject, was blotted out. In ordinary retrograde amnesia the memory gap would certainly have been more complete and less selective. The selectiveness of the gap is certainly in favor of a defensive repression—isolation and denial.

As to the problem of weak versus strong defenses in catatonic schizophrenia, the catatonic patient certainly does not do as well with electric shock as one might surmise from some statements in the literature. I shall talk about that soon before the Massachusetts Psychiatric Society. The results are not as perfect as one might hope for because of that very fact—the defenses in schizophrenia are enhanced and alerted. Schizophrenic patients, therefore, do better on insulin coma, which first lowers the defenses and then helps the patient reorganize them in a more balanced manner. Catatonic patients react relatively better to electric shock than do patients with some other types of schizophrenia, because their severer regression is a relatively less effective defense. I should grade regression as a poor defense. However, statistically speaking, even catatonic patients do only slightly more than half as well as depressive patients.

Dr. Jossmann's question is an interesting one, namely, why defensive repression did not come into play against the experiment itself. The reason may be that this man had an unreasonable lack of fear in regard to it and a strong desire to undergo it. My generally encouraging manner with patients may have added to his lack of fear. But the most important point seems to me that there was desire to have punishment because he was smarting under a recent experience of failure, although he had obviously rationalized that away. I believe, however, that he did not repress the shock because he had wanted to receive shock.

Abstracts from Current Literature

EDITED BY DR. BERNARD J. ALPERS

Physiology and Biochemistry

EFFECT OF INTRAVENOUS PAPAVERINE HYDROCHLORIDE ON THE CEREBRAL CIRCULATION. H. W. JAYNE, P. SCHEINBERG, M. RICH, and M. S. BELLE, J. Clin. Invest. **31**:111, 1952.

The purpose of this paper was to report the observations on the effects of intravenous injection of papaverine on central blood flow and metabolism in 18 subjects, as measured by the nitrous-oxide technique.

The authors found that intravenous administration of papaverine hydrochloride, in doses of 0.2 gm. injected in 20 minutes, resulted in a 13% increase in cerebral blood flow, a commensurate decrease in arterial cerebral venous oxygen difference, with no change in cerebral oxygen consumption, and a decrease in cerebral vascular resistance and cerebral venous oxygen tension. It is their belief that the mechanism whereby papaverine increases cerebral blood flow and decreases cerebral vascular resistance is its direct vasodilating effect on cerebral vessels.

ALPERS, Philadelphia.

RECOVERY FROM THE DECEREBRATE STATE ASSOCIATED WITH SUPRATENTORIAL SPACE-TAKING LESIONS. H. FREEDMAN, J. Neurosurg. **9**:52 (Jan.) 1952.

The exhibition of the decerebrate attitude has always been recognized as of grave prognostic import, especially when it comes in the course of supratentorial space-taking lesions. It has been the opinion of many that the supervention of the decerebrate attitude militates against, if not actually precludes, the possibility of recovery regardless of therapy. This report presents evidence indicating that prompt definitive surgery may be followed by survival and, in many instances, by complete recovery.

The 19 patients selected for this report were studied over a period of three years. In all instances supratentorial lesions were present and recovery followed appropriate surgical therapy.

In 14 cases bilateral extensor rigidity was present, and in the remainder there was involvement of one or both extremities on one side. The underlying conditions included subdural hematomas, 12 cases; temporal lobe tumor, 2 cases; frontal lobe abscess, 1 case; epidural hematomas, 3 cases, dissolution of a temporal lobe following contact trauma of the head, 1 case. In each case operative treatment consisted of evacuation of the mass. In most cases, improvement following surgery was continuous, but in two instances evidence of rigidity reappeared after various intervals and again disappeared after further appropriate surgical treatment.

The degree of recovery varied from absence of any residual symptom to severe and incapacitating defects requiring continued institutional confinement. In 13 of the 19 cases of this series the outcome was reasonably satisfactory. It is of interest to note that there was no correlation between the duration of the decerebrate attitude prior to operation and the eventual outcome and that both the patients who had repeated periods of decerebration made satisfactory recoveries.

In summary, Freedman points out that it seems well established that the decerebrate state associated with supratentorial space-taking lesions is a result of impairment of circulation in the brain stem secondary to herniation of the medial aspect of the temporal lobe through the incisura tentorii (the temporal pressure cone). He emphasizes the fact that any sign indicative of dysfunction of the midbrain occurring during the course of a supratentorial space-taking lesion should be a signal for immediate definitive surgery.

ALPERS, Philadelphia.

LUMBAR DISC PROTRUSION: A USEFUL SIGN. D. MCEACHERN, J. Neurosurg. **9**:229 (March) 1952.

McEachern reports a helpful sign in some cases of protrusion of a lower lumbar disk. When localizing tests and myelography give no clue, the sign may lead to successful surgical exploration and removal of the offending disk.

The skin over the back on the affected side is very sensitive to the prick or stroke of a pin or to rough tactile stimulation. The sensation is described as "spreading," "vibration," or painful; always as unpleasant and unusual. In this respect it resembles "thalamic" overresponse. The responsive area usually extends from the lower costal margin to the iliac crest, behind, and occasionally down onto the buttock, or even onto the sacral area on the back of the thigh and leg. On the loin it extends forward only to about the posterior axillary line and does not involve corresponding segmental areas on the anterior abdominal wall. It is therefore not segmental in distribution.

Strong reflex contraction of the posterior spinal or intercostal muscles of the affected side may accompany stimulation of the skin, even when the stimulus is insufficient to cause unpleasant sensation.

The phenomenon seems to be a referred hyperalgesia and is not due to root involvement. It disappears at once after operation. A possible explanation may be in the intersegmental nerve supply of the dura and ligamentous structures.

ALPERS, Philadelphia.

WATER EXCHANGE OF CENTRAL NERVOUS SYSTEM AND CEREBROSPINAL FLUID. E. A. BERING, J. Neurosurg. **9**:275 (May) 1952.

A complete study of each component of the cerebrospinal fluid is necessary before the dynamic physiology of the fluid can be accurately described. This paper presents a study of its largest component, water. With deuterium oxide (D_2O, heavy water) as a tracer, the water-exchange mechanism between blood and brain and cerebrospinal fluid was studied in the normal and in the hydrocephalic brain.

Bering found that water exchange between the blood and brain and cerebrospinal fluid occurs at a molecular level. The accumulation of cerebrospinal fluid is an independent phenomenon.

Equilibrium is established very rapidly between the brain and spinal cord and blood after intravenous injection of D_2O. The appearance of D_2O in the cerebrospinal fluid occurs simultaneously in the cerebral ventricles, the cisterna magna, and the spinal regions, at a rate that is governed by the surface area-volume ratio of any compartment considered.

The choroid plexuses are unimportant in the major D_2O exchange of cerebrospinal fluid. Circulation of cerebrospinal fluid through an intact subarachnoid pathway is not necessary for water exchange into and out of the cerebrospinal fluid, brain, or spinal cord.

Since water exchange offers no explanation of hydrocephalus or of why cerebrospinal fluid must flow, more investigation into the other components of cerebrospinal fluid is necessary.

ALPERS, Philadelphia.

ALTERATIONS OF BASAL GANGLION TREMOR DURING SLEEP. W. J. FRIEDLANDER, Neurology **2**:222 (May-June) 1952.

In an attempt to understand what happens to Parkinsonian tremor during sleep, the resting tremor of six patients with basal ganglion disease was compared with that of a normal (control) group (four subjects) while awake and while asleep.

Though Parkinson noted persistence of tremor in advanced cases of "shaking palsy" during sleep, many authors have commented on the disappearance of tremor during sleep. From the present study it would seem that the slow, typical tremor disappears during sleep, although the patients' disease may not have been at an advanced enough stage to permit an unequivocal conclusion. However, of greater interest was the appearance of a tremor during sleep the characteristics of which were indistinguishable from the tremor of the control group during sleep, which, in turn, was the same as that of the control group while awake.

Friedlander suggests that centers in the central nervous system maintaining wakefulness have a role in the production of Parkinsonian tremors which they do not have in the maintenance of normal tremor.

The depth of sleep in these studies was measured by the electroencephalogram. There seemed to be no relation between the electroencephalographic pattern and the frequency of a tremor.

ALPERS, Philadelphia.

EFFECT OF CHOLINE ON NEUROMUSCULAR TRANSMISSION IN THE CAT. O. F. HUTTER, J. Physiol. **117**:241, 1952.

In decerebrate and anesthetized cats intravenous injection of choline blocks neuromuscular transmission. In doses below the blocking level choline causes fibrillation and repetitive firing of the muscle, in response to single nerve volleys. Close arterial injections of choline have the same effects and, in addition, elicit a contraction of the muscle. In preparations blocked by tubocurarine the most striking action of choline is to restore neuromuscular transmission, and large doses are required to produce block. Records of end-plate potentials from the gracilis muscle showed that both an increase in the peak voltage and a lowering in the threshold voltage required for initiation of propagated responses contribute to the decurarization. The neuromuscular block and the reduction in threshold observed can be ascribed to depolarization at the motor end-plate region by choline. The increase in the end-plate potential must, however, be due to another mechanism. It is suggested that choline may increase the output of acetylcholine from the motor nerve-endings. No change in the time course of the end-plate potentials could be detected when choline was given. Choline, therefore, does not act by inhibiting cholinesterase. The question whether choline is ever normally present at the neuromuscular junction in a concentration sufficient to have any of the effects here described is discussed.

THOMAS, Philadelphia.

Neuropathology

LESIONS OF THE CORPUS LUYSII WITH DESTRUCTION OF THE HOMOLATERAL RED NUCLEUS WITHOUT HEMIBALLISMUS. J. NICOLESCO and T. NICOLESCO, Rev. neurol. **80**:677 (Nov.) 1948.

Nicolesco and Nicolesco observed a case of a posteroanterior, through-and-through bullet wound of the head which destroyed the corpus Luysii and nucleus ruber, as determined by serial whole sections of the brain studied with stains for myelin. Clinically, the patient presented numerous other signs, namely, bilateral difficulties referable to the pyramidal tract, left-sided sensory difficulties, left-sided intention tremor, pendular deep reflexes, nystagmus, Parinaud's syndrome, pseudobulbar disturbances, and psychic difficulties. Numerous other structures were destroyed, as well as the corpus Luysii and red nucleus, i. e., the vermis, quadrigeminal bodies, dentorubrothalamic radiations, and many structures surrounding the red nucleus and in the hypothalamus, as well as in the frontal lobe. Though there was no major hemorrhage along the bullet track, the interruption of vessels caused distant areas of softening.

The authors believe that hemiballismus is a release phenomenon of the extrapyramidal system caused by removal of the control of the corpus Luysii, but that this release occurs only with an intact extrapyramidal proprioceptive arc, in which the red nucleus is a link.

LEGAULT, Washington, D. C.

HEREDOATAXIA WITH DEMENTIA, EPILEPSY, MYOCLONIA, AND ARACHNODACTYLY: REPORT OF A CASE. G. MYLE and L. VAN BOGAERT, Monatsschr. Psychiat. u. Neurol. **118**:364, 1949.

Myle and van Bogaert report the case of a woman aged 24 who presented malformation of the teeth and skull, with a type of trophic disorder of the extremities described as arachnodactyly. There was evidence of dementia developing on the basis of oligophrenia. Neurologic examination revealed an ataxic gait, difficulty in standing and speaking, ataxia in performing the finger-to-nose and heel-to-knee tests, a positive Holmes phenomenon, and hyperactive deep reflexes, with paraparesis of the lower extremities and left ankle clonus. Epileptic seizures occurred once or twice a month and could not be controlled by medication. Clonic movements of various muscle groups, involving especially the muscles of the neck and shoulder girdle and the muscles of the lower extremities, might be continuous for days. The movements were asynergic and arrhythmic and might predominate on the right or the left side of the body.

Histopathologic study revealed small foci of cellular rarefaction apparently related to functional vascular disturbances, as well as necrosis of the cornu Ammonis and lamellar lesions of the cerebellar cortex. There were also degeneration of the posterior and lateral columns of the cord adjacent to the medulla and degeneration of the total olivocerebellar system, with an early transsynaptic degeneration of the dentate nucleus.

PISETSKY, New York.

Psychiatry and Psychopathology

THE FACE-HAND TEST AS A DIAGNOSTIC SIGN OF ORGANIC MENTAL SYNDROME. M. FINK, M. GREEN, and M. B. BENDER, Neurology **2**:46 (Jan.-Feb.) 1952.

In the course of sensory studies by the method of double simultaneous stimulation, it has been observed that patients with mental changes may show perceptual errors which are not demonstrable by routine single stimulation. When stimuli are simultaneously applied to the cheek and the hand (face-hand test), patients frequently report only one of the two stimuli, or, when reporting the two stimuli, mislocalize one to another part of the body, or even into space. These changes in perception are seen in repeated trials of the face-hand test and seem to form a consistent part of the syndrome usually labeled "organic mental syndrome," or "organic psychosis."

This report is based on a study of 400 patients who manifested cerebral dysfunction in the form of an organic mental syndrome, due to a variety of causes. These observations on the face-hand test in patients with organic disease of the brain were compared with previously obtained results of similar examinations in normal adults and children and in adult patients with schizophrenia.

It was found that patients with an organic mental syndrome make persistent errors in tests with double simultaneous stimulation of the face and hand. The errors are usually made in the hand. These errors are made on multiple trials of the face-hand test and on subsequent examinations on repeated days. The normal and the schizophrenic adults, however, do not make persistent errors.

The authors conclude that the face-hand test has clinical value. It furnishes a diagnostic sign of the organic mental syndrome. The persistence of errors on face-hand tests in an adult strongly suggests an organic mental syndrome.

ALPERS, Philadelphia.

AN INVESTIGATION OF THE PSYCHIATRIC ASPECTS OF DISSEMINATED SCLEROSIS. R. T. C. PRATT, J. Neurol., Neurosurg. & Psychiat. **14**:326 (Nov.) 1951.

An investigation was made by Pratt of 100 patients with disseminated sclerosis and of 100 control patients with regard to premorbid personality, emotional antecedents of the illness, and psychiatric, emotional, and intellectual changes following the illness.

No specific premorbid personality type could be defined in patients with disseminated sclerosis. Emotional stress antedating the onset or relapse of disseminated sclerosis was considered to be of occasional significance. A significant number of patients with disseminated sclerosis stated that an emotional stress, often of a specific nature, led invariably within the lapse of a minute to an exacerbation of symptoms due to a preexisting lesion.

Anxiety, hysteria, and psychosis were found not to be features of disseminated sclerosis. However, emotional lability and intellectual impairment were found in a significant proportion of patients with disseminated sclerosis, especially in those with pronounced neurological disability.

ALPERS, Philadelphia.

Meninges and Blood Vessels

ANTHRAX MENINGITIS: REVIEW OF THE LITERATURE AND REPORT OF TWO CASES WITH AUTOPSIES. T. H. HAIGHT, Am. J. M. Sc. **224**:57 (July) 1952.

Haight reports two cases of anthrax meningitis. One patient was a wool sorter in whom cutaneous anthrax developed, followed in five days by meningitis despite treatment with penicillin. He died 24 hours after the onset of cerebral signs. The second patient had no anthrax lesions outside the nervous system. She died despite aureomycin therapy. The organism was isolated in the spinal fluid of both patients. A brain abscess was found in the second case.

BERLIN, Mount Vernon, N. Y.

STREPTOCOCCAL MENINGITIS FOLLOWING DIAGNOSTIC LUMBAR PUNCTURE. D. P. BAUMANN and L. C. KOCH, Ann. Int. Med. **36**:1090 (April) 1952.

A young man in good health was subjected to a routine diagnostic lumbar puncture. Within 18 hours there developed acute infectious meningitis due to a microaerophilic Streptococcus, which subsided with massive penicillin therapy.

There are probably several routes whereby a virulent organism can be carried to the meninges by means of a lumbar puncture. In the experimental animal a lumbar puncture performed within a few minutes of the injection of a large quantity of virulent organisms into the blood stream will almost invariably result in a meningitis due to the injected organism. The theory has been advanced that the sudden lowering of the spinal fluid pressure in some manner breaks down the blood-brain barrier. Another hypothesis is that the needle, passing through small venous or capillary channels, carries organisms from the circulating blood directly to the meninges at the site of injection.

In the case reported there was no preexisting septicemia. The organisms therefore must have been introduced into the spinal canal by means of the needle. This either was improperly sterilized or was contaminated as it passed through the skin by organisms which had not been eradicated by the ordinary means of antisepsis. The authors believe the latter was the source of infection in this case.

ALPERS, Philadelphia.

CLINICAL COMPLICATIONS OF CEREBRAL ANGIOGRAPHY. K. H. ABBOTT, J. R. GAY, and R. J. GOODALL, J. Neurosurg. **9**:258 (May) 1952.

The purpose of this paper is to summarize the untoward effects of cerebral angiography as the authors encountered them clinically in 150 cases in which they performed cerebral angiography (174 angiograms). In this group serious untoward complications were encountered in 17 cases, with 5 fatalities. In two instances less serious, though alarming, signs were noted. Case reports detailing these major complications are given.

The clinical complications of cerebral angiography are summarized, and the etiological factors involved in their production are discussed. The means of avoiding complications, as well as their treatment, are summarized.

Abbott and his colleagues suggest that (1) percutaneous angiography is the method of choice, and probably is followed by fewer complications; (2) thorotrast® is the medium of choice in those cases in which degenerative or inflammatory cerebrovascular disease is suspected; (3) iodopyracet (diodrast®), though irritating to the vascular endothelium, is comparatively harmless in low concentrations and small quantities.

Cerebral angiography is not an altogether innocuous procedure, but it is an important advance, and an addition to the diagnostic methods available in intracranial disease when it is used with certain precautions and technical skill. The immediate recognition and treatment of complications associated with its use are imperative, and many times therapy will be successful.

ALPERS, Philadelphia.

Diseases of the Brain

VARIABLE OPHTHALMOPLEGIA DUE TO ANGIONEUROTIC EDEMA. W. E. FRY and N. S. SCHLEZINGER, A. M. A. Arch. Ophth. **46**:655 (Dec.) 1951.

Angioneurotic edema as the cause of ophthalmoplegia is extremely rare. Because of this, Fry and Schlezinger report a case.

A married white woman aged 25 had a family history of allergies in both parents and in a maternal uncle. Repeated examinations of the patient at various intervals verified the impression that there were pronounced, unpredictable alterations in her abnormal neuro-ophthalmological status. At one time there were partial ptosis of the left eyelid and limitation of external gaze bilaterally, as well as limitation of upward gaze in the left eye. Three days later there were marked edema of the right eyelid and almost complete ptosis of the right lid, with deviation of the right eye downward and inward. During the next three days, the edema subsided but the ptosis of the right lid persisted, and it was noted that when the left eye was covered the right eye could be brought back to the primary position from the deviated position downward and

inward. As the edema subsided, the skin of the right eyelid appeared brawny and desquamating. Twelve days after this episode, only slight palpebral edema remained, with slight ptosis of the left eye and upward and outward deviation of the right eye. A similar episode developed 24 days later, with initial involvement of the left eye, but within 48 hours the condition had spread to involve the right eye similarly. Fourteen days later there was complete subsidence of the edema, but with evident ptosis of the left eyelid and with limitation of outward and upward gaze of the left eye.

The patient was investigated for evidence of sensitivity by the scratch and intracutaneous methods. The examiner was skeptical as to whether the elimination and the avoidance of reacting proteins would afford relief. Nevertheless, a diet was recommended on the basis of this study, and the patient was advised to avoid inhalants as much as possible. Since she manifested a rather strong immediate reaction to histamine and Staphylococcus toxoid, as well as a delayed reaction to the latter, a course of hyposensitization with Staphylococcus toxoid, as well as an attempt to build up tolerance to histamine, was arranged. Since the patient soon became pregnant, it was not possible to maintain direct supervision and observation from an allergic standpoint.

The authors state: "Angioneurotic edema tends to be resistant to therapy unless a specific allergic factor is discovered and can be eliminated; as a rule epinephrine and ephedrine are ineffective; spontaneous recovery has been said to occur with advancing age, and the prognosis is said to be relatively better in the cases in which hereditary predisposition is lacking."

SPAETH, Philadelphia.

INTRANASAL ENCEPHALOCELES: SURVEY OF PROBLEMS, WITH RECOMMENDATIONS FOR REDUCING MORTALITY. E. WALKER, W. W. MOORE, and J. R. SIMPSON, A. M. A. Arch. Otolaryng. **55**:182 (Feb.) 1952.

Intranasal encephalomeningocele probably occurs much more frequently that is indicated by the number of reported cases. A review of the literature indicates that the occurrence of intranasal encephalocele has been associated with an extraordinarily high mortality. The principal causes of this high rate in the past have been failure to appreciate the nature of the lesion and ill-advised intranasal procedures, which have resulted in meningitis.

The first essential in reducing the mortality is a correct diagnosis. Any nasal tumor discovered in a newborn baby or a child is likely to be an encephalocele, since polyps and neoplasms are rare in children. The pedicle always leads to the superior limit of the nasal sulcus. The mass itself often protrudes from one nostril and may be visible in the pharynx. It is soft and compressible and may weep cerebral fluid. Though it may be cystic, aspiration is hazardous because of the risk of meningitis. Rhinorrhea is frequently evident, and the root of the nose may be distended by the intranasal mass.

The authors advise against any intranasal procedure which may initiate leakage of cerebrospinal fluid, once the diagnosis has been made. Adequate chemotherapy should be instituted. If any significant nasal obstruction exists, a tracheotomy is indicated. Intracranial repair of the cerebrospinal-fluid communication should be performed as the primary operation. If there is any persisting nasal obstruction, it can be relieved by the intranasal removal of the hernial mass.

In their view of the literature, Walker and his colleagues found a total of three cases in which intracranial repair of an intranasal encephalocele was successfully carried out. They present their case of the lesion in a baby girl which was similarly treated, with a successful outcome.

ALPERS, Philadelphia.

CUTANEOUS NEUROFIBROMATOSIS (VON RECKLINGHAUSEN'S DISEASE). F. W. PRESTON, W. S. WALSH, and T. H. CLARKE, A. M. A. Arch. Surg. **64**:813 (June) 1952.

Sixty-one patients with cutaneous neurofibromatosis were studied, with particular reference to associated lesions of other organs. Osseous changes and mental disorders each occurred in 20% of the cases; ocular disorders and other congenital defects, in 18%. Brain tumors were present in 14%, and spinal cord tumors, in 5%.

Sarcoma was one of the most serious complications, with an incidence of 16% in this series. The sarcomas associated with neurofibromatosis are rarely cutaneous but arise from deeper

structures. They have a poor prognosis even after radical extirpation, since they tend to recur locally or to metastasize. On the other hand, extirpation of benign cutaneous neurofibromas carries no risk of later malignant degeneration, nor is neurofibromatosis per se a contraindication to surgery.

LIST, Grand Rapids, Mich.

ELECTROENCEPHALOGRAPHIC CHANGES IN PROFESSIONAL BOXERS. E. W. BUSSE and A. J. SILVERMAN, J. A. M. A. **149**:1522 (Aug. 23) 1952.

The syndrome of boxing encephalopathy is probably due to multiple concussion hemorrhages, as well as to contusion and laceration of the brain. If the trauma sustained is severe, or is mild but repeated at intervals that do not permit the brain to return to normal functioning, permanent damage may result.

Many investigations have been reported on the value of the electroencephalogram in the detection of brain injuries. In the state of Colorado regulations have been set up by the state athletic commission as follows: 1. A professional boxer must have an electroencephalogram at least once a year. 2. In the case of a "knock-out" an electroencephalogram must be done within two weeks of the injury. 3. Frequent repeated examinations should be done in the case of a boxer with a suspicious recording.

The purpose of this article is to record, as an initial report, the results obtained with the first year's electroencephalograms in Colorado and to attempt to evaluate the worth of the electroencephalogram in safeguarding the health of those who participated in boxing.

Compulsory electroencephalographic examinations were made on 24 professional boxers. A statistically signicant increased incidence of dysrhythmic electroencephalograms was found in nine boxers (37.5%) in this series. There was some indication that men who had been knocked out showed severer electroencephalographic disturbances than those who had not been knocked out. Focal disturbances were more frequent in the younger men than in the older men, who also, generally speaking, had fewer electroencephalographic disturbances.

Busse and Silverman present the case of a boxer who was finally suspended from boxing largely on the basis of progressive electroencephalographic abnormalities. From their findings they conclude that periodic, compulsory electroencephalographic examinations contribute to the protection of boxers and should be a required part of routine examinations.

ALPERS, Philadelphia.

VASCULAR LESIONS IN PITUITARY ADENOMAS. C. F. LIST, J. R. WILLIAMS and G. W. BALYEAT, J. Neurosurg. **9**:177 (March) 1952.

The authors present another aspect of the kaleidoscopic pituitary syndrome, viz., the vascular lesions occurring in pituitary adenoma.

Pituitary adenomas occasionally tend to undergo vascular changes, such as massive hemorrhage or infarction. The resulting clinical syndrome is dramatic and puzzling, as the adenoma may previously have produced minimal or no symptoms. There is acute onset of grave intracranial signs, such as subarachnoid or intracerebral hemorrhage. Blindness or extraocular paralyses may rapidly develop. Secondary signs of acute panhypopituitarism (with adrenal insufficiency) frequently complicate the picture. The cerebrospinal fluid either is bloody or may show moderate polymorphonuclear pleocytosis. Roentgenograms of the skull disclose typical intrasellar erosion. Carotid angiography may be required to differentiate the condition from bleeding intracranial aneurysm.

If severe loss of vision or extraocular paralyses have developed, early operation is indicated, provided there are no signs of acute hypopituitarism. If, however, the clinical syndrome is dominated by evidence of severe panhypopituitarism, surgical treatment is inadvisable, and even x-ray treatment is dangerous; supportive hormonal therapy should then be given.

The authors report three cases with good outcome. In two treatment was surgical, and in the third, with radiation and hormones.

ALPERS, Philadelphia.

MEMORY DEFECTS AFTER HEAD INJURY. M. WILLIAMS and O. L. ZANGWILL, J. Neurol., Neurosurg. & Psychiat. **15**:54 (Feb.) 1952.

Retrograde amnesia, usually of short duration, is almost invariably present in cases of closed head injury of sufficient intensity to produce some period of post-traumatic amnesia. In addition to the residual retrograde amnesia, even when this is extremely brief, there may be further weakness in the memory for events which have occurred before the injury. In this paper Williams and Zangwill analyze the incidence and character of these memory defects in six cases in which the patient appeared to have made a complete recovery from head injury. They indicate that in some cases, despite lack of residual impairment in tests of memorizing and intelligence, faulty recall of pretraumatic events may be serious enough to constitute a minor residual disability.

The principal dysmnesic features shown were (*a*) gaps in memory for events leading up to the accident, yet not falling within the duration of retrograde amnesia; (*b*) hazy and ill-defined recollection of events which had occurred up to a week or more before the accident, and (*c*) disturbances in the recall of sequence of recent events.

A further study was made of 24 cases of closed head injury from the point of view of residual memory defects of the kind described. In two-thirds of the cases there was evidence of a memory defect extending beyond the duration of retrograde amnesia as clinically ascertained. It was found that, regardless of the length of post-traumatic amnesia, patients with retrograde amnesias longer than a few seconds are more likely to have other memory defects of the type described than those with retrograde amnesia lasting only a few seconds.

The authors conclude that the full extent of memory defect for events preceding the injury is not necessarily given by the duration of retrograde amnesia as conventionally ascertained. It appears there are two separate aspects of the memory disturbances following head injury: (1) the short, and usually complete, retrograde amnesia, and (2) more diffuse and widely distributed disturbances of memory for pretraumatic events. An evaluation of both these factors might be of value in assessing the progress of recovery and in leading to a more accurate appraisal of the extent of general cerebral disturbances.

ALPERS, Philadelphia.

FOCAL ENCEPHALITIS WITH PNEUMOENCEPHALOGRAPHIC FINDINGS RESEMBLING THOSE OF SPACE-OCCUPYING LESIONS. J. A. GHERSI, N. E. PIACQUADIO, and A. FERNANDEZ, Prensa méd. argent. **39**:355 (Feb. 22) 1952.

A patient admitted to the hospital with a history of progressive weakness of the right lower extremity of two month's duration revealed right hemiplegia, predominantly crural, with pyramidal tract signs on that side, and weakness of the right lower part of the face. Jacksonian seizures ending in loss of consciousness, were noted during hospitalization. Air studies showed a space-occupying lesion on the left side of the brain; there was no papilledema. The patient improved spontaneously. A third pneumoencephalogram, done 25 days later, showed a dilated ventricle on the left side. The authors assume the existence of a focal encephalitis of viral origin.

N. SAVITSKY, New York.

NEUROLOGIC DISTURBANCES WITH ACHYLIA GASTRICA. H. M. CANELAS, Arq. neuro-psiquiat. (March) 1952.

Canelas studied 53 patients with gastric achylia and neurologic changes. Thirty-one were men and 22 women; 47 of the patients were white persons; 3, Negroes, and 3, mulattoes. Fifty-two complained of paresthesias. Nineteen of the 52 had diminished sensation with a peripheral-nerve pattern. Twelve had tenderness of the calves. In five dissociated sensory changes were found, indicating intramedullary involvement. Two patients presented alterations in electrical excitability of the muscles. No case of muscular atrophy were noted. One patient had facial diplegia. Twenty-two had only posterior-column involvement. In one the only objective finding was diminished vibration. Sixteen patients presented dissociation of vibration and position sense. No patient had segmental sensory changes with normal vibration. If the methods used for checking vibration sense are precise, changes can be picked up much earlier. The author suggests the value of using the biothesiometer for measuring the threshold of vibration sense. Proprioceptive changes were severer in the lower limbs. It was noted

that the level of the spine below which the vibration could not be felt was important as a base line in studying the progression or regression of sensory changes. The Babinski sign was found bilaterally in 30.2% and unilaterally in 20.8% of patients. Rossolimo and Mendel-Bechterew reflexes were noted in 7.5% of the patients. Three patients had decubitus ulcers. Eleven manifested mental changes—agitation, hallucinations, and depression. Four had achylia gastrica and neurologic changes indicating involvement of the spinal cord, but no hematologic changes. Seven patients who were given folic acid showed no increase in the severity of changes in the central nervous system. The author actually noted improvement in neurologic manifestations in five of the seven patients who were given this vitamin. He points out that improvement in paresthesias, and even some increase in motor power, may not be indicative of actual clearing up of neurologic manifestations. Such changes may take place as a result of a general improvement.

Gastric juice permits organisms to multiply in the gastrointestinal tract which otherwise are inhibited. Toxins and incompletely disintegrated proteins in the gastrointestinal tract also act on the central nervous system on an allergic basis. In addition to treatment with vitamin B_{12}, liver, and folic acid, the author suggests intrathecal injection of vitamin B and A, antihistamine therapy, and even administration of corticotropin.

N. Savitsky, New York.

Diseases of the Spinal Cord

Nontraumatic Cervical Dislocations in Rheumatoid Spondylitis. D. Kornblum and H. H. Nash, J. A. M. A. **149**:431 (May 31) 1952.

Spontaneous cervical dislocation may occur in the course of rheumatoid spondylitis and is of insidious onset, with progressive development of rotation and flexion deformities. The dislocation takes place during an active phase of rheumatoid disease, when hyperemia and capsular distention in the region of the cervical joints and deforming muscle spasm are important causative factors. When recognition is prompt, vigorous treatment in an early stage can prevent the fixed deformities resulting from such dislocations and relieve signs and symptoms of spinal cord compression.

Kornblum and Nash describe the cases of four patients. The first patient, a man aged 23, presented left unilateral dislocation of the atlas upon the axis. Skull traction was maintained for 4½ months, without reduction of the dislocation. Surgical attempts at correction were not deemed advisable, since the deformity was a unilateral dislocation which allowed ample room for the spinal cord. At no time did the patient have any definite neurological symptoms or signs referable to the dislocation.

The second patient was admitted with a complaint of nuchal pain radiating to both arms. Roentgenograms of the cervical portion of the spine revealed anterior dislocation of the atlas upon the axis. Skull traction was maintained for six weeks. Symptoms disappeared. A supportive back and neck brace was worn. Eight months later he was still asymptomatic, and roentgenograms demonstrated maintenance of the reduction.

The third patient was admitted with complaints of anorexia, loss of weight, weakness, and cervical and thoracic back pain. X-ray examination disclosed rheumatoid involvement of all the articulations of the cervical spine, with a 2-mm. forward subluxation of the fifth cervical articulation on the sixth cervical vertebra, which was not recognized at that time. Six months later a progressive increase in his cervical deformity was noted. He complained of radiating pain in the right shoulder and arm. Two weeks later he reported numbness and tingling in the arm and hand. No abnormal neurological signs were elicited. A second roentgenogram showed a 2-cm. forward dislocation of the fifth cervical vertebra on the sixth, with about 30 degrees of kyphotic and right lateral angulation and marked encroachment upon the neural canal. Skull traction was applied for 12 weeks, after which the patient was made ambulatory by a supportive brace. His severe radiating pain disappeared completely during the first week of traction and did not return.

The fourth patient had had joint pains for five years, and for the past two years had noted stiffness of the neck and tingling paresthesias in both hands. X-ray examination demonstrated

a 5-cm. forward dislocation of the sixth cervical vertebra on the seventh. This dislocation appeared to be of long standing because of calcific bridging anteriorly across the interspace between these bodies. The patient did not desire hospitalization or treatment.

ALPERS, Philadelphia.

RECURRENT LEFT LARYNGEAL NERVE PARALYSIS IN ARTERIOSCLEROTIC HEART DISEASE. S. ZELMAN and G. W. NICE, J. A. M. A. **149**:1291 (Aug. 2) 1952.

Hoarseness due to paralysis of the left recurrent laryngeal nerve is a rare occurrence in patients with congestive heart failure due to any cause, but is most commonly seen with severe mitral stenosis, and less commonly with congenital heart disease, when marked dynamic dilatation of the left pulmonary artery compresses the nerve against the aortic arch, its adjacent lymph nodes, and the ligamentum arteriosum. It is extremely uncommon in patients with arteriosclerotic heart disease, since the primary cardiac strain in such patients is nearly always on the left ventricle. Only when the arteriosclerotic left ventricle fails does increased pressure occur in the left auricle and the pulmonary vessels.

Zelman and Nice describe such a case in which left ventricle failure had been continuous, though varying in degree, for nearly four years. The patient was admitted on two occasions during that time with evidence of failure and, in addition, complete paralysis of the left vocal cord. While digitalization and treatment with mercurial diuretics did not entirely relieve his left heart failure, the hoarseness and paralysis of the vocal cords cleared repeatedly.

An additional factor in the compression of the recurrent laryngeal nerve in this case may have been the unusually low position of the aortic arch in relation to the left pulmonary artery.

ALPERS, Philadelphia.

SYNDROME OF THE ANTERIOR SPINAL ARTERY. A. T. STEEGMANN, Neurology **2**:15 (Jan.-Feb.) 1952.

The onset of this syndrome is sudden or rapid with girdle-like pain, followed by loss of perception of pain, touch, and temperature and by motor paralysis below the level of the lesion in the spinal cord. Motor paralysis at the level of the lesion is of the lower motor neuron type, but is of the upper motor neuron type below the level. A disturbance of bladder function occurred in all cases, with early retention, and in severe cases an uninhibited neurogenic bladder was a residual defect. Voluntary bladder control was reestablished in a few weeks in most cases. The lesion occurred in the lower cervical portion of the spinal cord in two cases, and in the midthoracic or the lower thoracic portion of the cord in the remainder. Syphilitic arteritis was the etiologic factor in two cases, arteriosclerosis in three cases, and infection in one case (that of the only young person, a 14-year-old girl).

Steegmann discusses the differential diagnosis. He points out that unless there is grossly bloody spinal fluid with or without spinal subarachnoid block, central hemorrhage into the spinal cord cannot be differentiated from thrombosis of the anterior spinal artery.

With modern treatment to prevent and control bladder infection and skin infections, and with early physical rehabilitation procedures, the prognosis of the anterior spinal artery syndrome is definitely better than it was a decade ago. The degree of permanent crippling depends on the amount of irreparable damage to the spinal cord.

ALPERS, Philadelphia.

CEREBRAL POLIOMYELITIS IN EARLY INFANCY. V. SMALLPIECE and C. OUNSTED, J. Neurol., Neurosurg. & Psychiat. **15**:13 (Feb.) 1952.

The first six months of life are generally considered to be a period of high immunity to poliomyelitis. This paper describes a small outbreak of poliomyelitis in a nursing home involving three infants, all probably infected from a common source, in whom the disease was followed by severe cerebral symptoms.

The patients were infants 7, 3, and 2 weeks of age. All had multiple lower motor neuron paralyses. One died in convulsion during the convalescent phase of the disease. One child survived for two years nine months but was idiotic, with multiple paralyses and fits. He died

after a seizure, and necropsy revealed the typical lesions of poliomyelitis in the spinal cord. One child was alive at the time of the report, but was also an epileptic idiot, with upper and lower motor neuron paralyses and athetosis.

The authors suggest that the midwife who attended the three children described in this paper was the vector. She was entirely healthy throughout the episode.

The clinical features and epidemiological aspects of cerebral poliomyelitis in early infancy are described and discussed.

ALPERS, Philadelphia.

NEUROLOGIC FINDINGS IN CASES OF CERVICAL DISK RUPTURE. P. F. GIRARD, Rev. oto-neuro-opht. **24**:39 (Jan.) 1952.

X-ray changes indicating the presence of ruptured cervical disk are found frequently in older persons. Such findings do not necessarily imply that the neurologic changes found in a particular case are discogenic. The author comments on the overemphasis given the role of pressure on the posterior roots in the early stages of herniated cervical disk. The first structure involved after herniation is the ligament. Pressure on these ligaments is important in accounting for pain. It is also responsible for the reflex spasm of the neck muscles, resulting sometimes in torticollis and hypotonus of the cervical paravertebral muscles, especially the trapezius. This accounts for the drooping of the shoulder and the costoclavicular region. Herniated cervical disk is often the cause of the scalenus anticus syndrome. The author believes that the changes in the cord and roots are due to accompanying arachnoiditis and arachnoidal cyst formation rather than to direct compression on these structures. He thinks that in some cases cervical pachymeningitis may be due to herniated disk. Two spinal cords from patients with herniated cervical disk were examined by the author. There was no evidence of direct compression. He found gliosis and degenerative changes in the vessels, and within the cord. Block was due to adhesions and cystic arachnoiditis rather than to the herniation of the disk. These facts undoubtedly explain the occasional poor results after operation in some cases. The author collected 15 cases of optic neuritis associated with redicular pain in the upper limb in which the ocular changes cleared up with traction. One cannot deny the role of herniated disk in the development of optic neuritis. This is probably due to pressure on the cervical anterior roots, through which autonomic fibers pass. These fibers supply intracranial blood vessels. Occasionally neuralgic pains in the upper limbs which have not been relieved by cutting the posterior roots disappear when the anterior roots are freed from pressure and adhesions. Frikholm has called attention to the necessity for examining and treating these changes in the region of the anterior roots.

N. SAVITSKY, New York.

CHRONIC REMITTING EPIDURITIS. B. B. SPOTA, C. A. BARDECI, and J. C. CHRISTENSEN, Prensa méd. argent. **39**:382 (Feb. 29) 1952.

An unusual case of remittent epidural infection is reported in a woman aged 31 with long-standing furunculosis of the neck and back. After an injury to the left knee, which was followed by hydrarthrosis, paresthesias in both lower limbs appeared, with complete spastic paralysis at the end of eight months. Examination revealed a sensory level for temperature and pain at the seventh thoracic dermatome, and absence of vibration sense to the pelvis. Complete subarachnoid block was found, and the fluid was xanthochromic and contained increased protein. The serologic reaction of the fluid was positive. The patient was treated with mercury and penicillin, with marked improvement. Absence of blood was demonstrated, and the Wassermann reaction in the spinal fluid was negative. Soon after admission to the hospital she began to improve and finally was able to return to work. She had no complaints, and there were no positive neurologic findings for two years and five months. Then, 10 days after an infection of the upper respiratory tract, paresthesia and weakness of the left lower limb reappeared. On readmission she was found to have a Babinski sign on the left, weakness and some atrophy of the left lower limb, and absence of the left knee jerk, but no objective sensory change. Despite two more months of antibiotic treatment, the weakness increased in the left lower limb, with later involvement of the right leg. Three months after recurrence there was paraplegia, with a bilateral Babinski sign, a sensory level at the third thoracic dermatome, and complete block. The Wassermann reaction of the spinal fluid was mildly positive. The myelogram

showed a block at the eighth thoracic level. Operation revealed extensive epidural infection, and a strip of granulomatous tissue 20 cm. long was removed. Postoperative x-ray therapy was given. Histologic examination showed chronic hyperplastic epiduritis with multiple microscopic abscess formation, but no evidence of syphilis. There was some improvement after operation and x-ray therapy, but the patient continued to present bilateral weakness and hypotonia in the lower limbs and some sensory diminution below the ninth thoracic level.

N. Savitsky, New York.

Peripheral and Cranial Nerves

Sciatica Caused by Tumoral Calcinosis. P. A. Reimenschneider and A. Ecker, J. Neurosurg. **9**:304 (May) 1952.

The purpose of this paper is to draw attention to sciatica caused by tumoral calcinosis. The condition is rare and of obscure etiology, marked by benign, lobulated, fluctuating, calcified cystic masses in the region of gliding surfaces or bursae. These masses are usually not accompanied by pain, tenderness, or limitation of motion.

In the case here presented, low-back and left sciatic pain with the clinical syndrome of a protruded intervertebral disk was caused by tumoral calcinosis. The symptoms were apparently the result of pressure by extruded contents of the cystic mass on the first and second sacral nerves within the spinal canal. The symptoms were promptly relieved by operation.

Alpers, Philadelphia.

Vertigo and Cervical Adenopathy. Mayoux, Chossegros, and Lafon, Rev. oto-neuro-opht. **24**:65 (Feb.-March) 1952.

The authors reported three cases in which a fairly clear relation existed between attacks of vertigo and cervical adenopathy. In the first case vertigo recurred each time there were swelling and flaring up of a tuberculous cervical gland. In the second case vertigo disappeared after a course of radium therapy to the cervical gland, involvement of which appeared secondary to epithelium of the face. In the third case vertiginous attacks disappeared after excision of a calcified gland near the carotid artery. The authors believe that the attacks of vertigo are a result of involvement by the enlarged gland of autonomic fibers which go to the inner ear. During an attack of vertigo in the first case retinal arterial pressure was 35 mm. on the left and 50 mm. on the right. Eight days after the vertiginous attack the retinal arterial pressure was equal on the two sides. The change in retinal arterial pressure is added evidence that during the vertiginous seizure there was significant impairment of the intracranial vasomotor system. In the third case carotid sinus dysfunction as a possible cause of the vertigo is suggested. The authors did not find any other similar cases in the literature.

N. Savitsky, New York.

Isolated Accommodation Paralysis Following Mumps. Beltz and Bouchel, Rev. oto-neuro-opht. **24**:159 (April) 1952.

Paralysis of accommodation after mumps is a rare complication. Previous cases have been reported, but the authors had never seen this complication, although they report having seen many cases of mumps. Mumps was diagnosed in a soldier aged 20. Eleven days later he complained of visual difficulties and was unable to read the newspaper. Orchitis appeared at the same time. On his admission to the hospital, 18 days later, the orchitis and parotitis had cleared up. The external appearance of the eyes, the ocular movements, and the fundi were all normal. Impaired vision was correctible by the use of lenses. There was no evidence of diabetes mellitus or diphtheria; the accommodation paralysis was not due to asthenia. The function of accommodation gradually returned to normal. For four days after admission there was mild meningeal irritation. No mention of lumbar puncture was made. The authors report that the pupils reacted well to light and in convergence. They note that the ocular complication in this case occurred during the first week, while the parotid glands were still enlarged, and lasted one month.

N. Savitsky, New York.

RECURRENT LARYNGEAL PARALYSIS IN CARDIAC DISORDERS: ORTNER'S SYNDROME. A. QUADRELLI, Prensa méd. argent. **39**:293 (Feb. 15) 1952.

Ortner reported laryngeal paralysis in association with mitral stenosis for the first time in 1897. This paralysis was considered due to pressure on the recurrent laryngeal nerve by the dilated left auricle and the aortic arch. Alexander, in 1904, suggested that laryngoplegia is due to compression of the recurrent laryngeal nerve by a dilated left pulmonary artery. Additional pressure against the nerve was considered possible by the pushing upward of the dilated auricle against the pulmonary artery. The author reports two cases of heart disease with recurrent laryngeal paralysis. In both cases there was evidence of heart failure with passive congestion of the lungs. One patient was a woman aged 45 with mitral stenosis; the other, a woman aged 54 with hypertension and heart failure; both had laryngeal paralysis. In the second the left auricle was not enlarged. The author considers that the recurrent laryngeal nerve involvement in both cases was due to pressure from a dilated left pulmonary artery. The nerve is compressed in the triangle formed by the arch of the aorta, superiorly, the left pulmonary artery, below, and the ligamentum arteriosum, medially. The dilated auricle in mitral stenosis may also play an accessory role by pushing the dilated pulmonary artery upward.

N. SAVITSKY, New York.

Vegetative and Endocrine Systems

LAURENCE-MOON-BIEDL SYNDROME. A. CSORBA, Confinia neurol. **10**:378, 1950.

Csorba reports cases of the complete Laurence-Moon-Biedl syndrome (retinitis pigmentosa, dystrophia adiposogenitalis, oligophrenia, and polydactyly) in three siblings. Genealogical studies suggested that the incomplete picture was present in some members of the maternal side of the family. The mother was healthy, but her sister and her grandfather had poor eyesight and oscillations of the eyes. In addition, her sister was the only plump member of a family of nine siblings and was considered the least intelligent. This kind of ancestral background has been present in other cases of the complete Laurence-Moon-Biedl syndrome.

FOLEY, Boston.

Treatment, Neurosurgery

TREATMENT OF PNEUMOCOCCAL MENINGITIS WITH LARGE DOSES OF PENICILLIN. P. A. BUNN and G. PEABODY, A. M. A. Arch. Int. Med. **89**:736 (May) 1952.

In 1941 Dowling and his group reported their observations on a series of 21 patients with pneumococcic meningitis who were treated with large doses of parenterally administered penicillin. Their observations indicated that a regimen of 1,000,000 units given by the intramuscular route every two hours resulted in an appreciable drop in mortality. The incidence of complicating sequelae and the total length of illness were also reduced.

Bunn and Peabody present a series of 20 patients with bacteriologically proved pneumococcic meningitis who were similarly treated with large doses of parenterally injected penicillin. They used and recommend the administration of a dose of 1,000,000 units every two hours for at least one week, or until clinical remission seems secure. They feel that the intrathecal use of penicillin is not desirable, for the reason cited by Dowling, viz., poor penetration to all areas of infection and the irritative qualities of the drug. They found that adjuvant therapy with a sulfonamide or aureomycin apparently adds nothing to the efficacy of the regimen, but point out that it is not contraindicated.

Of the 20 patients in this series, 15 recovered and 5 died, 3 within 24 hours of hospitalization. None of these three received more than 12 doses of penicillin. The other two patients, aged 82 and 83, died after receiving therapy for 12 and 15 days, respectively. In both patients evidences of meningeal infection had subsided, and death was due to other causes.

Fifteen patients survived and were free from all evidence of meningitis. Residua referable to the central nervous system occurred in only two patients. The seventh-nerve paralysis in one was not of major importance and did not preclude a complete return to active life. The vestibular and auditory defects in the second patient gradually cleared, and after six months there was no significant loss of either function.

Twelve surviving patients in this series received therapy for 6 to 19 days. Treatment was extended 24 to 40 days for three other patients because of the persistence of chronic middle ear infection and abscess of the eye. During the period of acute meningitis, spinal fluid concentrations of 0.05 to 0.5 unit per cubic centimeter were obtained with 1,000,000 units of penicillin given intramuscularly. Blood concentrations reached peak levels of 5 to 20 units with this dose.

ALPERS, Philadelphia.

SOME ASPECTS OF HISTAMINE IN MÉNIÈRE'S DISEASE. N. G. RICHTNER, A. M. A. Arch. Otolaryng. **55**:434 (April) 1952.

Fifty-three cases of Ménière's disease were studied with reference to histamine as an etiologic factor and as to its value in treatment. Routine intradermal tests, according to Atkinson's method, with 0.01 mg. of histamine dihydrochloride, were carried out, and reactions were read after 5, 10, 15, and 20 minutes, applying Atkinson's criteria. At the same time blood samples were taken for determination of the histamine content. The purpose was to study the blood histamine content in Ménière's disease and to see whether any correlation existed between high blood levels of histamine and histamine-positive skin reactions.

These investigations of histamine in the blood were based on the possibility that a certain liberation of histamine may occur from the tissues to the blood in acute attacks of Ménière's disease, and that this increased content may be present in the blood for a time. As a rule, it was not possible to make histamine determinations during acute attacks; they were made mostly in the intervals between, or a day or so after, the acute attacks. For purposes of comparison, blood histamine determinations were made on 40 patients with otosclerosis and on 9 controls.

It was found in this series that histamine skin tests gave positive reactions according to Atkinson's criteria in about 15% of the patients with vertigo. The mean blood histamine value was not higher in patients with vertigo than in normal persons and patients with otosclerosis; rather, the values were somewhat lower, and were lowest in persons presenting positive histamine reactions.

Only a few persons in this series were treated with histamine, and the effects seemed to be very indefinite, as far as could be judged. However, Richter feels that histamine plays a part in Ménière's disease and that its role merits further investigation and research.

ALPERS, Philadelphia.

CARE OF SEVERELY PARALYZED UPPER EXTREMITIES. R. L. BENNETT, and H. R. STEPHENS, J. A. M. A. **149**:105 (May 10) 1952.

The purpose of this paper is to outline methods of care of the patient with severe flaccid paralysis of the upper extremities and to discuss ways of increasing functional capacity through the use of adaptive apparatus.

In this study, 324 postpoliomyelitis patients with permanent severe weakness of the upper extremities were treated at the Georgia Warm Springs Foundation.

As for all involved body segments, treatment during the early stages of convalescence consists of protection and support, gradually increased mobilization and muscle stimulation and reeducation in all involved segments.

If, after a period of four to six months of adequate treatment, the shoulder, arm, forearm, and hand show no muscle strength above a "trace" to a "poor minus" level, it is assumed that further muscle reeducation will not bring back significant functional strength. It is possible to provide mechanical apparatus which will permit the patient to feed himself, have independence in personal hygiene, write or type, and use the telephone. Such apparatus is here illustrated. The restoration of some degree of independence to these patients with paralyzed upper extremities is most gratifying.

ALPERS, Philadelphia.

AGRANULOCYTOSIS RECURRING DURING PHETHENYLATE ("THIANTOIN") SODIUM THERAPY. A. E. HUSSAR and H. B. ROGERS, J. A. M. A. **149**:1312 (Aug. 2) 1952.

All the newer anticonvulsants, with the exception of diphenylhydantoin sodium, are capable of depressing bone marrow in an occasional case. The authors here present the first known direct evidence of toxic effects of phethenylate on the bone marrow.

Agranulocytosis developed in their patient on the 20th day of administration of phethenylate ("thiantoin") sodium, 2 grains (0.13 gm.) twice a day. After cessation of treatment with the drug, the patient promptly recovered. The advisability of frequent blood cell counts during the administration of the newer anticonvulsants is emphasized by Hussar and Rogers.

ALPERS, Philadelphia.

FOCAL EPILEPSY OF PSYCHOMOTOR TYPE: A PRELIMINARY REPORT OF OBSERVATIONS ON EFFECTS OF SURGICAL THERAPY. J. R. GREEN, R. E. H. DUISBERG, and W. B. MCGRATH, J. Neurosurg. **8**:157 (March) 1951.

During a two-year period, 23 patients, each manifesting psychomotor epilepsy which failed to respond to systematic medical therapy, and presenting spontaneous electroencephalographic spiking in the anterior temporal area, were studied surgically.

Selection of these patients for surgical intervention was made on the basis of a careful evaluation of the history and the clinical, electroencephalographic, and electrocorticographic findings.

Gross or microscopic pathologic changes were found in association with the electrographic disturbances in the anterior portion of the affected temporal lobe in 14 of the 23 patients. In general, these patients were benefited more by surgical measures than were patients in whom no lesion was found. In selected cases of psychomotor epilepsy, temporal lobectomy, anterior to the receptive acoustic cortex, appears to be more effective than lobotomy or gyrectomy.

All 23 patients are living. Of the 23 patients, 12 have had no psychomotor seizures since operation. The neurologic deficits following anterior temporal lobectomy were surprisingly few in this series and are described.

The authors discuss the effects of anterior temporal lobectomy on seizures, the electroencephalogram, and the mental status, and the clinical elements that appear to be associated with favorable and unfavorable results. They believe that radical excision offers hope for selected patients who have definite clinical and electrographic localization and whose attacks are not controlled by medication.

ALPERS, Philadelphia.

SURGICAL TREATMENT OF PRESACRAL TUMORS: A COMBINED PROBLEM. C. S. MACCARTY, J. M. WAUGH, C. W. MAYO, and M. B. COVENTRY, Proc. Staff Meet., Mayo Clin. **27**:73 (Feb. 13) 1952.

The authors present the problem of treating sacral and presacral tumors, describing their procedure in 10 cases. When the diagnosis of a sacral or presacral tumor is established, certain steps are carried out before operation to reduce the incidence of wound infection and to prepare the lower part of the colon and the rectum for possible resection if such an eventuality proves necessary. The patient is hospitalized, and preparation of the colon is begun. This usually requires three days. Antibiotics are given the day before operation and continued for five days after operation. While the preparation of the colon is being made, special neurological tests are conducted to ascertain whether the tumor is encroaching on the cauda equina.

At operation an abdominal surgeon mobilizes and protects the rectum and pelvic organs. An orthopedic surgeon and a neurologic surgeon resect the tumor from the ligaments and surrounding muscles. The orthopedic surgeon osteomizes the sacrum and ilium. The neurologic surgeon attempts to identify and preserve the sacral roots, and pudendal and sciatic nerves. If there is intraspinal and subarachnoid extension, he handles these problems.

By utilizing the special assets of these three surgical specialties the authors believe they have evolved a method best suited to dealing with these tumors.

ALPERS, Philadelphia.

TREATMENT OF THE ACUTE PAINFUL PHANTOM LIMB. L. C. KOLB, L. M. FRANK, and E. J. WATSON, Proc. Staff Meet., Mayo Clin. **27**:110 (March) 1952.

"Phantom limb" is a term used to designate the sensation of perception of the presence of an extremity following its amputation. Pain in the phantom extremity is uncommon. Kolb and his colleagues had the opportunity of studying and treating three patients in whom the phenomena of painful phantom limbs developed immediately after amputation, and they report two of these cases.

Although physiologic mechanisms contribute, it is clear to the authors that the painful element is a symptom which is maintained by psychic mechanisms and may be understood only by some comprehension of the patient's past experiences, in particular, those that relate to the development of his attitudes toward his body. They found that a brief rational psychotherapy may be effectively applied to relieve the painful symptoms and associated panic.

In addition, the authors suggest that proper preparation of a patient who is to undergo amputation might prevent in some instances the development of the painful-phantom hallucination. Such preparation could be carried out by the surgical team and would include a discussion of the occurrence of the phantom phenomena and a considerate inquiry as to the patient's wishes and fears in regard to the disposal of the part to be amputated.

ALPERS, Philadelphia.

TRAUMATIC LESIONS OF THE INTRACRANIAL OPTIC PATHWAYS. G. M. FASIANI and A. BEDUSCHI, Riv. oto-neuro-oftal. **26**:411 (Sept.-Oct.) 1951.

Fasiani and Beduschi report the results in 17 cases in which operation was performed for relief of impairment of vision following head injuries. Six were instances of immediate amaurosis following the accident (five unilateral). No results were obtained from operations on the optic canal. These operations were done 20 days to 2 months after the accident. The poor results were probably due to the delay of operation on the canal. Streiff suggests operating within four days after the injury if the patient's condition permits. While in most cases complete blindness immediately after the head blow is due to irreversible tearing of nerve tissue, it occasionally is due to edema and hemorrhage. In these cases early decompression of the optic canal may be of great benefit. The authors also report recovery of vision in two cases and improvement in six cases after liberation of adhesions around the optic nerve and chiasm. Operation was performed in 12 cases of post-traumatic optochiasmatic arachnoiditis. The authors do not advise operation while the patient is in coma. The exploration of the optic pathways should always be by the intracranial route. The authors believe that the optic sheath should also be incised to facilitate decompression.

N. SAVITSKY, New York.

EFFECT OF ELECTRIC SHOCK IN GLAUCOMA AND RETINITIS PIGMENTOSA. G. PENTINI, Riv. oto-neuro-oftal. **27**:144 (March-April) 1952.

Electric shock therapy was given in four cases of glaucoma and in five cases of retinitis pigmentosa. Temporary improvement was noted in some of the cases. The diagnosis of glaucoma was unquestionable in only three of the four cases. There was temporary improvement of visual acuity, field restriction, and intraocular tension. In all cases improvement lasted only one to five months. In one of the cases visual acuity and intraocular tension remained unaltered. However, the temporal field returned to normal, and there was widening of the nasal field by 10 degrees. In the second case the intraocular lesion returned to normal after the birth treatment, the visual field widened 50%, and there was improvement of vision. In the third case there was only a slight widening of the field after electric shock; the intraocular tension increased.

In four of the five cases of retinitis pigmentosa there was some improvement of vision and field restriction decreased. Improvement in these cases was slight, and perhaps within the limits of spontaneous remission. The changes in these cases was also transitory, lasting a few months.

To test the hypothesis that electric shock therapy may produce transitory improvement in ocular diseases by its effect on the diencephalohypophyseoadrenal system, the author studied circulating eosinophiles and the uric acid-creatinine ratio before and after electric shock therapy. These studies were done in six of the nine cases; eosinopenia and some increase in uric acid-creatinine ratio point to the probability of increased adrenal activity soon after electric shock therapy.

N. SAVITSKY, New York.

Muscular System

DYSTROPHIA MYOTONIA. ALFANDARI, Harefuah **42**:6 (Jan. 1) 1952.

Alfandari reports three cases of dystrophia myotonia which were observed, respectively, in two sisters aged 40 and 37 and in a man aged 30. The author reports that generalized and focal weakness may appear before atrophy of the limbs and that myotonia is sometimes absent in early cases. It usually does not interfere with walking or other motor activities. Myotonia is usually found only on examination. It is readily detected by clasping the hands of the patient or by mechanical stimulation. It is usually found in the tongue and the thenar muscles. Myotonia may also be elicited electrically. In one of the reported cases the myotonic reaction appeared only after the patient had been under observation four years. The author noted edema of the biceps in one case, a change not previously noted in the literature on myotonic dystrophy. In all three cases weakness preceded the atrophy in the lower limbs. In two of the cases weakness began in the lower limbs. In two of the three cases weakness was more pronounced in one lower limb than in the other. A cataract was seen in only one of the three cases and appeared in the fourth year of the illness. A cataract may at times be the only manifestation of the disease in other members of the family. Frontal baldness was not present in any of the cases. In one case a muscle biopsy showed inflammatory reaction, in addition to atrophy of muscle fibers.

N. SAVITSKY, New York.

CHRONIC POLYMYOSITIS. E. CHRISTENSEN and H. LEVISON, Acta psychiat. et neurol. **25**:137, 1950.

Christensen and Levison report on six patients with polymyositis without involvement of the skin. The patients included four women, of ages ranging from 16 to 38; a man aged 41, and a boy aged 9 years, probably stricken from birth. Three patients had a picture similar to that of progressive muscular dystrophy, with proximal atrophy and weakness of the limbs and a typical waddling gait. Several patients had severe pains in the leg, thigh, or shoulder muscles. Generally the proximal muscle groups were affected. Muscle biopsy in all six cases showed inflammatory infiltration of the interstitial connective tissue with polymorphonuclear leucocytes, lymphocytes, plasma cells, and a few eosinophiles. In four cases the round cell infiltration was chiefly perivascular, and in two cases it was very diffuse. The muscle fibrils in the individual bundles showed irregular atrophy. Electromyography in five cases indicated some type of myogenic disorder. The creatinine output was increased in four patients and normal in one. Treatment consisted of administration of large amounts of penicillin or streptomycin. In a patient treated with penicillin there was an exacerbation, with death following acute myocarditis. In three patients treated with streptomycin there seemed to be some effect on pain, atrophy and paresis.

PISETSKY, New York.

Encephalography, Ventriculography and Roentgenography

A SCINTILLATION COUNTER FOR THE DIAGNOSIS AND LOCALIZATION OF INTRACRANIAL NEOPLASMS. M. TER-POGOSSIAN, W. B. ITTNER, W. B. SEAMAN, and H. G. SCHWARTZ, Am. J. Roentgenol. **67**:351 (March) 1952.

The authors describe in some detail the apparatus they have developed and use for localization of brain tumors which have selectively taken up radioactive diiodofluorescein. In this method of localization of brain tumors it is the gamma radiation emitted by radioactive iodine (I^{131}) which must be counted. The scintillation counter is better for this purpose than the Geiger-Müller tube because it is more efficient in counting gamma rays. The authors estimate that their apparatus is about 40 times as efficient in counting gamma rays as the conventional Geiger tube with a bismuth cathode. This increased efficiency makes possible much shorter counting times while retaining the same statistical accuracy of counting as the Geiger tube. If desired, the dose of radioactive material given the patient can be lowered appreciably, and the counting times will remain within entirely practical limits.

The authors use a crystal of sodium iodide with the addition of a small amount of thallium impurity as the source of the scintillations. They believe it is more efficient for this work

than calcium tungstate crystals. Patients receive an intravenous dose of 0.25 mc. of radioactive diiodofluorescein, and counting begins 20 minutes later. The total time required for a survey of 32 locations on the skull is about 15 minutes. The authors find that the instrument they use is stable and reliable in their hands.

WEILAND, Philadelphia.

UNCOMMON COMPRESSING LESIONS OF THE SPINAL CORD AND ITS MEMBRANES. A. SHEINMEL and S. M. GLASSER, Am. J. Roentgenol. **67**:415 (March) 1952.

Sheinmel and Glasser report five cases in which unusual lesions caused compression of the spinal cord and the diagnoses were made by myelography, with the x-ray diagnosis later verified by surgical exploration. Of the five cases, two were of adhesive arachnoiditis; one, of angiomatous malformation of the spinal cord; one, of herniated nucleus pulposus, causing a complete block in the myelogram, and one, of infectious myelitis, with edema of the cord.

WEILAND, Philadelphia.

CRANIAL CLUES TO INTRACRANIAL ABNORMALITY. WILDER PENFIELD, Am. J. Roentgenol. **67**:535 (April) 1952.

Penfield points out that it is the duty of the clinician to search for the cause of attacks in all cases of epilepsy. Each case eventually will be classified as one either of idiopathic epilepsy or of focal epilepsy. It is primarily the cases of focal epilepsy with which the paper deals. The focal seizures arise in abnormal living gray matter. They do not originate in tumors, cysts, and the like, although they may arise in the gray matter immediately adjacent to these abnormalities. The neurosurgeon who intends to treat focal epilepsy must use every available means to localize the lesion. "When he has made a reasonably accurate localization he may hope to stop the seizures completely in a little over 50 per cent of the cases and decrease the attacks in others."

Asymmetry of the cranium supplies a clue to injury to the brain which occurred during infancy and childhood, the active period of brain growth. The cranium is smaller over the damaged side, and often the paranasal sinuses and mastoid air cells become larger on the same side, as though to take up the space left by failure of growth of the damaged part of the brain.

Atrophic lesions of the brain often produce changes in the size, shape, and position of the ventricles. These changes may be demonstrated by pneumoencephalography. In some cases of damage during infancy the ventricle on the side of the lesion may become very large; in others it shows little change. Atrophic lesions acquired after brain growth is complete (i. e., in adults) regularly produce enlargement of the ventricle on the same side. The contralateral ventricle is almost always enlarged also, but to a slightly less degree.

Intracranial calcifications may be associated with focal epilepsy. Calcification may appear in slow-growing brain tumors, tuberculomas, healed brain abscesses, and in a peculiar sort of lesion which Penfield has called "hemangioma calcificans." Occasionally actual plaques of bone may be found located in the subdural or subarachnoid spaces in cases of focal epilepsy. These are thought to be associated with previous hematomas in the same region. Trauma to the underlying area of the brain is probably caused by the same force that produced the hematoma.

Superficial cysts or tumors of the brain may make their presence known by producing thinning of the cranium which overlies them. Meningioma often causes formation of new bone in the overlying portion of the skull. When there is a deficiency in the dura, perhaps caused by trauma or by surgery, the brain can rather quickly produce an irregular, "pebbly" erosion of the cranium overlying it. This is so even if the pia and the arachnoid lie intact between the brain and the skull. Penfield has named this defect in the skull "craniocerebral erosion." In the presence of increased intracranial pressure the erosion occurs more rapidly.

WEILAND, Grove City, Pa.

FORAMINA PARIETALIA PERMAGNA. R. O'RAHILLY and M. J. TWOHIG, Am. J. Roentgenol. **67**:551 (April) 1952.

The parietal bone ossifies in membrane from one or more centers in the region of the future parietal eminence. The spread of ossification toward the median plane is slower in the region of the future parietal foramen. A membranous interval, called the "sagittal fontanelle," is thus

left in this region. The parietal emissary vessels pass through the lateral angle of this membranous space. As ossification proceeds in this region, a parietal foramen is left as a remnant of the membranous space. Foramina parietalia permagna may be considered to arise as a delay in an otherwise normal process of ossification.

The parietal foramen is present in about 60% of persons. It is most commonly unilateral. More than 90% of human parietal foramina do not exceed 1 mm. in diameter. Large parietal foramina have been associated by various authors with cranial anomalies, such as metopism, microcephaly, synostosis of sutures, plagiocephaly, and thinness of the parietal bones.

O'Rahilly and Twohig present short reports of five cases in which large parietal foramina were found. The large foramina were an incidental postmortem finding in the first case, that of a man aged 75. The foramina in this case were bilateral, and each was approximately 1 cm. in diameter. In the other four cases the foramina were found on roentgenograms of the skull. Three of these four cases were found in one family. Reexamination of the three patients over a period of eight years showed little change in size or appearance of the large parietal foramina. The largest ones were about 3.5 cm. in diameter when measured on the roentgenograms.

WEILAND, Grove City, Pa.

SYMMETRICAL CALCIFICATION IN THE CEREBELLUM. A. B. KING and D. M. GOULD, Am. J. Roentgenol. **67**:562 (April) 1952.

King and Gould encountered two cases in which roentgenograms of the skull presented the appearance of calcification within the dentate nuclei of the cerebellum. In both cases the calcification was fairly dense and well visualized on the skull films. The first patient, a white man aged 64, had syphilis of the central nervous system. He had received malaria therapy. No other abnormal intracranial calcifications were noted in the roentgenograms of his skull. When the brain was examined post mortem, dense serrated deposits of calcium were found in the dentate nuclei. There was also fine linear calcification in the surrounding white matter of the cerebellum.

The second patient, a white woman aged 52, had osteitis deformans (Paget's disease of bone) and Ménière's disease. Roentgenograms of the skull showed dense calcification in the region of the pineal body and two symmetrical coarsely linear calcific deposits in the region of the dentate nuclei. The calcified pineal body was in normal position.

In neither case could any symptoms or physical signs be ascribed to degeneration of the dentate nuclei, nor were there any apparent clues concerning the cause of the calcification in either case.

WEILAND, Grove City, Pa.

Congenital Anomalies

ARNOLD-CHIARI MALFORMATION. L. I. MALIS, I. COHEN, and S. W. GROSS, A. M. A. Arch. Surg. **63**:783 (Dec.) 1951.

The authors describe in detail three cases of their own in which the malformation was successfully treated surgically. The paper contains excellent photographs of the operative findings and myelograms showing the deformity. The authors feel that the Arnold-Chiari malformation is primarily a developmental anomaly which may lead to hydrocephalus. This, in turn, increases the deformity. In addition, a low fixation of the spinal cord, e. g., by a lumbomyelomeningocele, may enhance the displacement of the hindbrain by requiring the neuraxis to assume an excessive length.

Among the various clinical features, the presence of radicular irritation at the level of the second cervical roots is emphasized. Association with bony deformity, such as platybasia, is common. To demonstrate the Arnold-Chiari malformation, myelography is considered the method of choice. Surgical treatment is recommended, consisting of suboccipital decompression and adequate cervical laminectomy. The dura should be left open, but excision of the anomalous cerebellum or aspiration of cervicomedullary cysts is unnecessary.

LIST, Grand Rapids, Mich.

News and Comment

FIFTH INTERNATIONAL CONGRESS ON MENTAL HEALTH

The World Federation for Mental Health has accepted the invitation of the Canadian Mental Health Association and the Canadian Psychological Association to hold the Fifth International Congress on Mental Health in Toronto, Canada, Aug. 14-21, 1954.

The World Federation for Mental Health was created in 1948 to promote better human relations and to increase understanding among cultures, among nations, and among professions. It is the only voluntary international organization of its kind so broadly conceived. The Federation grew out of and replaced an older body, known as the International Committee for Mental Hygiene. By creating a body with a new name, it was hoped to express a broad conception of interdisciplinary partnership in human relations rather than to lay primary stress on mental illness, and to emphasize the fundamental importance of planning for preventive work.

The Federation has consultative status with UNESCO and the World Health Organization and is on the register of the Secretary-General of the United Nations as a body to be consulted by the Economic and Social Council.

The members of the Federation are mental health associations and professional societies. These cover the major fields concerned with mental health, human relations, and intercultural understanding and include medicine, psychiatry, psychology, cultural anthropology, sociology, and social work, education, and nursing. There are 72 member societies, from 38 countries, and the total number of technically trained persons who are members of these associations of the Federation approximates 1,000,000. Many persons are also affiliated with the Federation as associates.

Four International Congresses have been held to date. The first two, in Washington, in 1930, and in Paris, in 1937, were under the auspices of the International Committee on Mental Hygiene. The Third Congress, held in London in 1948, had as its theme "Mental Health and World Citizenship." It was out of this congress that the World Federation for Mental Health developed. Since that time the Federation has held annual meetings in Geneva, Paris, México, D. F., and Brussels. The Fourth International Congress on Mental Health was held in México, D. F., Mexico, in December, 1951.

The Fifth International Congress is to be held at the University of Toronto, Aug. 14-21, 1954. The program of the Congress is being planned to reflect advances in the field of mental health and to assist in realistic planning for the future. The theme of the Congress is Mental Health in Public Affairs.

Inquiries about the Congress should be sent to The Executive Officer, Fifth International Congress on Mental Health, 111 St. George St., Toronto, Canada.

AMERICAN ASSOCIATION OF PSYCHIATRIC CLINICS FOR CHILDREN FELLOWSHIPS

Fellowships offering specialized training in child psychiatry are available in a number of member clinics of the American Association of Psychiatric Clinics for Children which have been approved as training centers by the Association. The training begins at a third-year, post-graduate level, with minimum prerequisites of graduation from medical school, a general or rotating internship, and a two-year residency in psychiatry—all approved. The majority of these clinics have also been approved individually by the American Board of Psychiatry and Neurology for a third year of training and for an additional year of experience.

This training is in preparation for specialization in child psychiatry, especially for positions in community clinics devoted wholly or in part to the outpatient treatment of children with psychiatric problems. At the completion of training, attractive openings are available in all parts of the country. Fellows receive instruction in therapeutic techniques with children in outpatient settings which utilize the integrated services of the psychiatric clinic team. Most of the clinics have a two-year training period, although a few will consider giving one-year training in special cases.

Fellowship stipends are usually in line with United States Public Health Service standards, that is, approximately $3,600, as these stipends come mainly from the Public Health Service. Stipends sometimes are paid by state departments of mental health, the individual clinics, and, occasionally, communities paying for the training of psychiatrists engaging to work in these communities at the end of their training. Special arrangments may be made occasionally to supplement the stipends by taking on other responsibilities locally, e. g., part-time work with the Veterans Administration or consultation to social agencies. A limited number of training centers can offer higher stipends.

The office of the American Association of Psychiatric Clinics for Children acts as a clearing house for applicants. Application may be made through this office or directly to the individual clinics. In all cases, acceptance of applicants for training is by the individual training centers.

For further information and for application forms, write Miss Marion A. Wagner, Administrative Assistant, American Association of Psychiatric Clinics for Children, 1790 Broadway, Room 916, New York 19.

THIRD ANNUAL INSTITUTE IN PSYCHIATRY AND NEUROLOGY

The Third Annual Institute in Psychiatry and Neurology, sponsored by the Veterans Administraton Hospital, Lyons, N. J., the New Jersey Neuropsychiatric Association, and the New Jersey District Branch of the American Psychiatric Association, will be held April 22 and 23, 1953, at the Veterans Administration Hospital, Lyons, N. J.

The program will include clinical demonstrations and medical exhibits.

The program for the scientific session on April 22 is as follows: Dynamics of the Cure in Psychiatry, Iago Galdston, M.D.; Recent Research Developments in Schizophrenia, William Malamud, M.D.; Simultaneous Tactile Tests in Normal and Abnormal Subjects, Morris Bender, M.D.

At the dinner, on April 22, Gregory Zilboorg, M.D., will speak on "The Humanitarian and the Therapeutic in Psychiatry."

At the scientific session on April 23 the following papers will be read: Relation of Endocrine Glands to Mental Disturbances, Francis Braceland, M.D.; Modern Methods of Treatment in Psychiatry, Kenneth E. Appel, M.D.; Modern Approach to Diagnosis and Treatment of Brain Tumors, Leo M. Davidoff, M.D.

The registration fee is $1.00. Military and full-time Veterans Administration personnel are exempt.

Additional information may be obtained from Crawford N. Baganz, M.D., Manager.

OPENING OF NEW PSYCHIATRIC INSTITUTE OF UNIVERSITY OF MARYLAND

The formal opening of the new Psychiatric Institute of the University of Maryland was held on Nov. 17, 18, and 19, 1952, at the new Institute, in Baltimore. The first day was devoted to formal exercises dedicating the Institute. The honorary degree of Doctor of Science was conferred on Ralph W. Gerard, Ph.D., M.D., professor of neurophysiology in the department of Psychiatry and professor of physiology, University of Illinois; John von Neumann, E.Ch., Ph.D., D.Sc., research professor of mathematics, Institute for Advanced Study, Princeton University, and Stanley Cobb, M.D., Bullard professor of neuropathology, Harvard Medical School. At the dedication dinner, on Nov. 17, Alan Gregg, M.D., vice-president of the Rockefeller Foundation, gave an address on "Information, Power, and Responsibility."

The second and third days were devoted to scientific meetings centered on the topic "Change in Behavior." The topic of the second day was "Factors Influencing Behavior," and the meeting was under the chairmanship of Dr. Ralph W. Gerard. Speakers on this topic included Dr. Holger Hyden, Gothenburg, Sweden; Dr. J. H. Quastel, Montreal, Canada; Dr. Rafael Lorente de Nó, New York; Dr. O. Hobart Mowrer, Urbana, Ill., and Dr. Stanley Cobb, Boston. Margaret Mead, Ph.D., New York, gave a public lecture entitled "An Anthropologist Looks at Contemporary Behavior."

The morning meeting of the third day dealt with "Medical Education and Change in Behavior," under the chairmanship of Dr. Alan Gregg. The following speakers participated: Dr. John R. Reid, Palo Alto, Calif.; Dr. Philipp Frank, Boston; Dr. Thomas Hale Ham,

Cleveland; Dr. George Saslow, St. Louis, and Dr. Jacob E. Finesinger, Baltimore. The afternoon meeting dealt with "Psychotherapy and Change in Behavior," under the chairmanship of Dr. John C. Whitehorn, Baltimore. Participants were Dr. Talcott Parsons, Cambridge, Mass.; Dr. Anatol Rapoport, Chicago; Dr. Robert Waelder, Philadelphia; Dr. Jerome Frank, Baltimore, and Dr. Maurice H. Greenhill, Baltimore.

The new Institute provides 102 beds for inpatient care, with three floors of the building devoted to outpatient clinic, research laboratories, and teaching facilities. The building is designed to emphasize psychiatric teaching, the integration of psychiatry with other medical disciplines, research in neurophysiology, medical education, and behavioral sciences, as well as provide clinic service. The Institute is under the direction of Dr. Jacob E. Finesinger.

TRAINING POSITION FOR EPILEPSY CLINIC

A one-year training position will be available in the Consultation Clinic for Epilepsy, University of Illinois College of Medicine, Chicago, beginning July 1, 1953.

The position is open to anyone interested in pediatrics or neurology who wishes to acquire special competence in epilepsy and clinical electroencephalography in order to establish a center for diagnosis, treatment, teaching, and research.

The post has been created with funds allocated by the United States Children's Bureau and the Illinois Division of Services for Crippled Children.

The period of the appointment is from July 1, 1953, to June 30, 1954, with a salary of $5,000.

Applications should be addressed to Dr. Frederic A. Gibbs, Department of Neurology and Neurosurgery, University of Illinois College of Medicine, 912 S. Wood St., Chicago 12.

ILLINOIS CIVIL SERVICE COMMISSION

A severe shortage of physicians, psychiatrists, and tuberculosis-control physicians still exists in several Illinois state hospitals.

Oral tests for Physician I, Psychiatrist I, and Tuberculosis-Control Physician I are held as often as enough persons apply. Illinois residence is not necessary for any of the positions.

Physicians and psychiatrists who complete three years of service with the Department of Public Welfare are eligible for an educational leave of absence with full pay to conduct research or study approved by the Department.

Additional information and application forms may be obtained from the Civil Service Commission, Armory Bldg., Springfield, Ill.

UNIVERSITY OF CALIFORNIA EXTENSION COURSE IN BASIC NEUROLOGY

Presented as "a background for the understanding of clinical problems encountered in neurological and psychological fields," a course in basic neurology is offered in Los Angeles this spring by the University of California Extension to graduates of approved medical schools and to graduate psychologists.

Meeting on each Monday evening, Feb. 16 through June 8, from 7 to 9 o'clock in the staff room on the fifth floor, main building of the Veterans Administration Hospital, 5901 7th St., Long Beach, Calif., the course will offer a survey of the organization and function of the central nervous system.

The first lecturer in the series, on Feb. 16, will be T. H. Bullock, associate professor of zoology at University of California at Los Angeles, who will talk on "The Evolution of the Nervous System."

Printed bulletins, with complete lecture programs and other information, are available on request to Thomas H. Sternberg, M.D., head of postgraduate instruction, Medical Extension, University of California, Los Angeles 24, to whom applications for admission should also be addressed. Fee for the graduate course is $75.

Books

Mental Deficiency. By Edgar A. Doll, Ph.D., Director of Research at Devereaux Schools, Devon, Pa. in "Encyclopædia Britannica." 1951 Printing. Encyclopædia Britannica, 30 N. Wacker Dr., Chicago 6, 1952.

Dr. Edgar Doll, who worked for many years with the education of mental defectives at Vineland Training School, Vineland, N. J., has set forth in his article one of the most comprehensive discussions, explanations, and clarifications of the term "mental deficiency" to be found anywhere. The article goes far to point out the roots of many outdated concepts of mental deficiency. He defines the modern view of mental deficiency as a condition rather than a disease, and he outlines the six following characteristics as accepted parts of the concept: (1) social incompetence, (2) mental incompetence, (3) deficiency or defects of development, (4) constitutional origin, (5) duration to adulthood, (6) essential impossibility of cure.

The article is complete in that it enters into the problem of classification, intelligence, and ranges of intelligence in social competency. Possibly one of the most important parts of the article is the section on clinical detection. This particular phase of the problem of mental deficiency is, at present, receiving considerable attention throughout because of the increased interest in those exceptional children who heretofore were forgotten or cast aside by superstition or ignorance. The total feeling one gets from reading the article is that Dr. Doll's message needs to be more general knowledge in order that it may help in reducing the cultural lag in understanding of the true nature of mental deficiency.

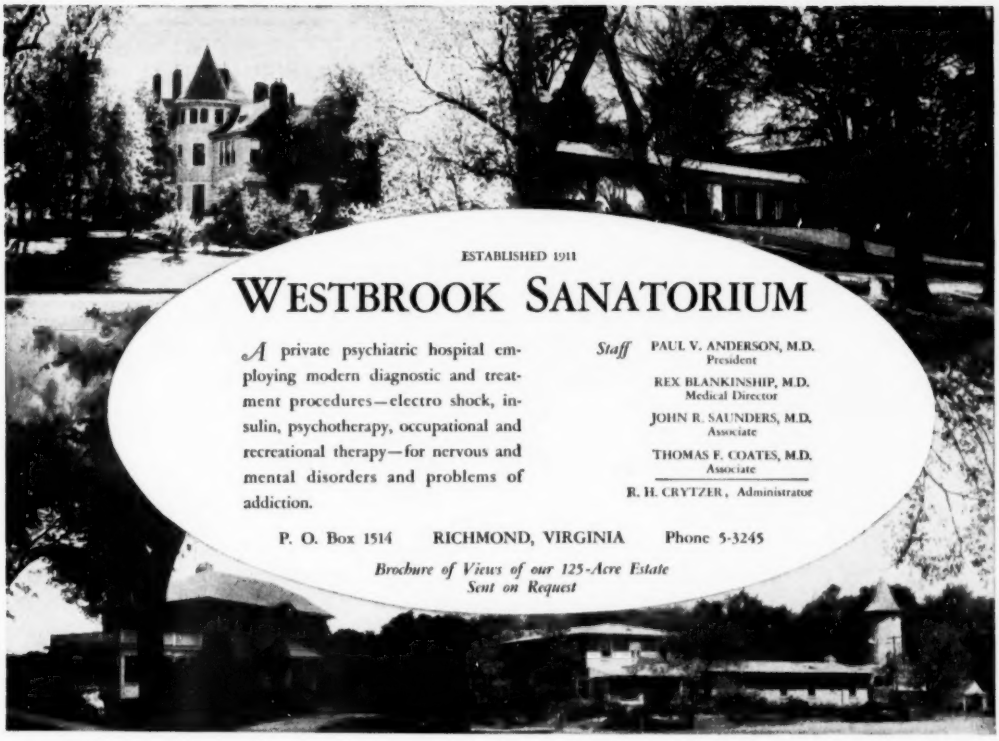
Personality and the Frontal Lobes. An Investigation of the Psychological Effects of Different Types of Leucotomy. By Asenath Petrie. Price, $6.50. Pp. 188, with illustrations. The Blakiston Company, 1012 Walnut St., Philadelphia 5, 1952.

One of the big gaps in our knowledge of psychological functioning after psychosurgery has been due to the inclusion of a smaller or larger number of schizophrenic subjects in the patient material. The psychosis in such studies "muddies the waters" so much that egregious errors have been registered. Mrs. Petrie has avoided this type of patient, and from McKissock's very large material has selected 70 neurotic patients for thorough preoperative and postoperative studies. Realizing that one leucotomy may be very different from another, she has also assessed the different types of leucotomy as performed by McKissock, comparing essentially the standard operation (plane of the coronal suture) with the anterior, or rostral, operation, in which the open approach is used, the medial half of the white matter of each frontal lobe severed under direct vision, and the incisions carried 2 cm. anterior to the sphenoidal ridge. A few patients were included who had only a right or a left rostral leucotomy. Those with left-sided operations approached the scores of the patients with bilateral rostral leucotomy.

The approach to the problem has been thorough, but the author is by no means dogmatic about her results and she drops hints that a lifetime of work would still leave questions unanswered. If there is anything really to criticize about her methods, it is the reliance upon the results of test situations. In other words, her patients are always responding to some problem placed before them. No measure is possible of their performance in the common situations of setting up their own problems and seeking their solution "for the hell of it." Tests are capably used that reveal reduction in neuroticism and in introversion. The results in all cases are outstanding. As far as intelligence was concerned, in the standard series verbal scores suffered much more than performance scores. Furthermore, while the decrease in neuroticism and introversion was substantial in the rostral cases, intellectual tests failed to reveal any deficit. The gimmick in the study was that the rostral leucotomy was not quite as successful as the standard operation in

restoring the patient to the highest degree of clinical improvement. Needless to say, all the patients examined were out of hospital and usefully occupied. "All the correlations between tests of intelligence and the success of the operation were of negligible degree."

Mrs. Petrie gives the test employed and the results obtained in such a manner that they can be repeated by those interested. Such examinations would require a total of something like six hours per patient—not excessive considering the subtlety of the personality alterations in these nonpsychotic patients. In addition to the test situations, however, she was able to gain further insight into her patients and to reveal some of her thinking along the lines of social interaction of leucotomized persons. In some ways this is the most interesting part of her essay. "Their vulnerability to the 'slings and arrows of outrageous fortune' has decreased. It may be that in this way they have lost the use of the barometer they previously had to gauge the climate of the reaction of others. The subtleties of human relationships—of what is painful and what is permissible—are constantly being impressed on us by our own experience in society. Being tactful is a much more complex form of behaviour than not hurting another person in the physical sense. . . . But the infliction of psychic pain depends on so many variables that we are constantly relearning the rules in our own relationship with the people round us. Perhaps leucotomy patients have difficulty for the reason suggested—their own decreased vulnerability to psychic pain—in relearning these rules."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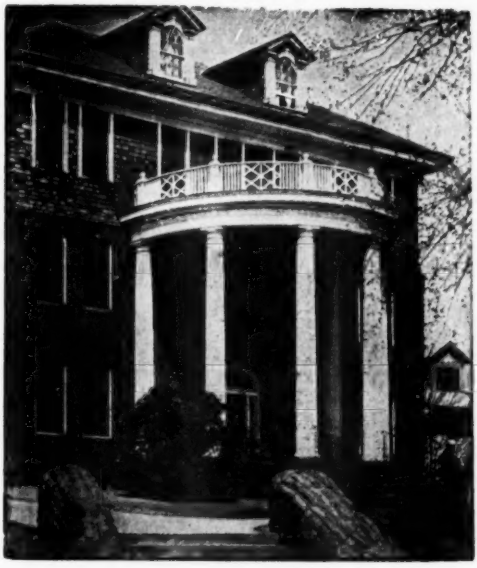

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